UNITED STATES DISTRICT COURT
DISTRICT OF MINNESOTA

CONFIDENTIAL

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In re:
Viagra Products Liability Litigation

MDL Docket No. 1724
Judge Paul A. Magnuson

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This Document Relates to:
Martin v. Pfizer
Stanley v. Pfizer

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VIDEOTAPED DEPOSITION OF CHERYL BLUME, Ph.D.
Taken on Behalf of the Defendant Pfizer Inc.

DATE TAKEN: February 12, 2009
TIME: 9:17 a.m. - 7:21 p.m.
PLACE: Pharmaceutical Development Group, Inc.
13902 North Dale Mabry Highway, Suite 122
Tampa, Florida

Stenographically Reported by:
Donna L. Peterson
Registered Diplomate Reporter
Certified Realtime Reporter

APPEARANCES:

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Also Present:
Jamie Hollingsworth, videographer

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PROCEEDINGS

THE VIDEOGRAPHER: Today's date is February the 12th, 2009. The time is approximately 9:17 a.m. My name is Jamie Hollingsworth. I'm the videographer. The court reporter is Donna Peterson.

We are present at the offices of Pharmaceutical Development Group in Tampa, Florida. We're here for the purpose of taking the deposition of Cheryl Blume, Ph.D. The case is instituted in the United States District Court, District of Minnesota. The short style is In re: Viagra Products Liability Litigation.

I will now ask the attorneys to introduce themselves, beginning with the plaintiffs' attorney.

MR. OVERHOLTZ: Yes. Neil Overholtz on behalf of the Plaintiffs Steering Committee.

MR. ALTMAN: Keith Altman on behalf of the Plaintiffs Steering Committee.

MR. BECNEL: Daniel Becnel on behalf of Plaintiffs Steering Committee.

MR. SPATZ: Mark Spatz for Pfizer.

MS. LESKIN: Lori Leskin for Pfizer.

THE VIDEOGRAPHER: Would the court reporter kindly swear in the witness.

CHERYL BLUME, Ph.D., called as a witness by the Defendant Pfizer Inc., having been first duly sworn, testified as follows:

THE WITNESS: I do.

JUDGE BORG: Dr. Blume, I'm the referee here.

THE WITNESS: Oh.

JUDGE BORG: If -- if anybody says "objection" when a question is asked of you, please hold up until I tell you whether or not you can do that.

If you don't understand the question, or if it isn't clear or if it's multiple or anything like that, and you want the question reasked, feel free to do that. Okay?

THE WITNESS: I will. And, I'm sorry, I didn't hear your name.

JUDGE BORG: It's John Borg.

THE WITNESS: Okay. Nice to meet you.

JUDGE BORG: Nice to meet you, too.

And any time that you need a break, just so say.

THE WITNESS: I will.

JUDGE BORG: And we'll take one. Okay?

THE WITNESS: Thank you.

JUDGE BORG: And we'll be breaking at about the one-hour mark every -- each -- each hour anyway.

THE WITNESS: Okay.

JUDGE BORG: Thank you.

DIRECT EXAMINATION

BY MS. LESKIN:

Q. Good morning, Dr. Blume.

A. Good morning.

Q. You're not an ophthalmologist, correct?

A. Correct..

Q. Is anyone on staff here at PDG an ophthalmologist?

A. No.

Q. Did you consult with any ophthalmologist in the preparation of your report in this case?

A.. No.

Q. You've never diagnosed ischemic optic neuropathy, correct?

A. No.

Q. Have you ever studied ischemic optic neuropathy prior to this litigation?

A.. Yes.

Q. In what concept -- in what context?

A. In association with a new development project that we are working on for a pharmaceutical client.

Q. Is that a current client?

A. It is.

Q. Is the new development project you're working

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on related to the treatment of erectile dysfunction?
A. No.
Q. Is the new development project you're working on a phosphodiesterase type 5 inhibitor?
A. No. It is an inhibitor of GABA-transaminase.
Q. As part of your work, have you determined the cause of anyone's ischemic optic neuropathy?
A. No. I was not asked to do that.
Q. You're not an expert in ocular blood flow, are you?
A. I mean, I've worked with ocular blood flow in my work, but ocular blood flow is not the focus of my career.
Q. When you say you've worked with ocular blood flow in your work, in what context?
A. The development program that we are working on impacts retinal blood flow.
Q. When did you start working on that project?
A. Approximately two and a half years ago.
Q. Have you ever published any articles on ocular blood flow?
A. No.
Q. Has anyone employed by PDG ever published any articles on ocular blood flow?
A. Well, I would have to check their publication

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lists, but I am not familiar with any.
Q. Okay. Is anyone on staff here, to your knowledge, an expert on ocular blood flow?
A. We do not have any ophthalmologists on staff.
Q. Do you have anyone who works with ocular blood flow on staff?
A. I would have to check their previous work, but their only experience at PDG is with the development program I discussed.
Q. You're not a medical doctor, right?
A. No. I'm a pharmacologist.
Q. And your Ph.D. is in pharmacology?
A. Correct.
Q. You don't diagnose patients' diseases, correct?
A. That is correct.
Q. Do you have any medical doctors on staff here at PDG?
A. We have had a medical doctor. He recently retired. And we are looking for another one.
Q. And when did he retire?
A. Oh, I'd have to check the records. It was in 2008, I believe.
Q. And what was his name?
A. Dr. Santalucio.
Q. And did Dr. Santalucio help you prepare the

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report in this case?
A. I'd have to check the billing records on that, but I do not believe so.
Q. You don't prescribe medications to patients, correct?
A. No. I'm a pharmacologist.
Q. And that, in fact, would be against the law in the state of Florida for you to write a prescription for a patient, correct?
A. Well, I've never checked that, but that would be my understanding.
Q. Okay. You've never worked for the FDA?
A. No.
Q. You've never served on an advisory committee for the FDA?
A. Well, I've always, over the last 30 years, represented industry, so I would not be eligible to be serving as an active member of the advisory committee. I have worked on two para-advisory committees with FDA, one on antihypertensives and one on the elaboration of electronic data submissions.
Q. Okay. You've identified that as a para-advisory committee. What do you mean by that?
A. Because it was directed — not directed toward the -- a particular drug product. It was more a process

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and a category of drugs, and not the approval of a pending NDA.
Q. You've never served on an advisory committee for the FDA, correct?
A. Correct.
Q. And you're not an epidemiologist, correct?
A. Of course we use epidemiology in our work, but my Ph.D. is in pharmacology.
Q. And so you personally are not an epidemiologist?
A. I personally am not an epidemiologist.
Q. Do you have epidemiologists on staff here at PDG?
A. Yes.
Q. And did that person help with the preparation of the report in this case?
A. In the review of literature, yes.
Q. And what's the epidemiologist on staff's name?
A. Darren Shearer.
Q. When were you first contacted about the Viagra litigation?
A. I believe it was the late summer, early fall of last year.
Q. 2008?
A. 2008.

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Q. And who contacted you?
A. I believe it was Mr. Overholtz.
Q. And what did Mr. Overholtz tell you at the time he first contacted you?
A. That they were working with, I believe it was with Viagra, and looking at different issues associated with Viagra, and they were interested in talking with me regarding a regulatory overview of those issues.
Q. Had you worked with Mr. Overholtz before?
A. Yes.
Q. In which litigations had you worked with Mr. Overholtz?
A. Baycol.
Q. Anything else?
A. I'm not recalling any as I sit here, but I would probably have to check my list, because oftentimes there are groups of attorneys who work with cases.
Q. Mr. Altman is here. You've worked with Mr. Altman before, correct?
A. Yes.
Q. On several litigations, right?
A. And in my product development work, yes.
Q. Okay. What litigations have you worked with Mr. Altman in?
A. Let's see.. Baycol. Neurontin. Mirapex. The

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fenfluramine litigation, fentanyl litigation, and isotretinoin. And there may be others, but those are the ones that immediately come to mind.
Q. Did you work with Mr. Altman on the hormone replacement therapy litigation?
A. I don't recall on that litigation, since it was largely a cancer end point, if we did an evaluation of the adverse event databases. But I may have, perhaps.
Q. And -- but you worked on the hormone replacement therapy litigation?
A. Yes.
Q. Did he work with you on Seroquel litigation?
A. No.
Q. Did you work on Seroquel litigation?
A. I recall consulting on it. I don't believe I've been designated as an expert in it.
Q. What question were you presented with in connection with the Viagra litigation?
A. As I recall, they -- the attorneys were interested in a review of the regulatory events relating to primarily the NDA for erectile dysfunction, looking at the events subsequent to the initial approval of the NDA, and examining, in a manner similar to what I do for product development when I'm helping a client with post-marketing work, a review of the literature

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following approval. A review of clinical studies or Phase IV-type studies that may have been done after approval, tracking of pharmacovigilance efforts following approval, looking at various adverse event databases, events outside the United States, if they were applicable to events inside the United States. An overview of the handling of adverse events and labeling information relative to what was going on at that particular time point as it relates to FDA, comparing that with other drug labeling.
Q. Okay. Walk me through the methodology that you went through to answer those questions.
A. Uh-huh. Multiple tasks are conducted when evaluating the postapproval events of a drug product. Of course the first that is done is an overview of the scientific literature. We conduct our own literature searches, our own literature surveys and evaluations. We don't rely on literature that is provided to us. I think in this case we accessed 3300 literature articles and had a working library, somewhat, of the retinal issues because of our work with the earlier development program. So the literature was reviewed.
We also did an overview of the regulatory events, relying on -- not only on the documents that were provided to us by counsel, but we independently

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accessed regulatory records in the United States. And if relevant, we will access them, also, from other countries.
We also examined the regulatory events relating to pharmacovigilance, so our -- we'll look at Phase IV work, Phase IV studies that were done or were not done. We asked Mr. Altman to evaluate the AERS database.
We then looked -- also looked at an overview of the labeling chronology. Our interest in this case was of course the ophthalmic event, so we reviewed the evolution of the labeling as it relates to ophthalmic events, both those events that were precipitated by your client, as well as those events that were triggered by the Food and Drug Administration.
We looked at other labeling during the relevant time period for these events to see how other companies may have handled these events, in their discussion points in the labeling, as well as if there was any patient labeling.
And we reviewed the documents that were provided to us, the company's documents that were provided to us, primarily from the perspective of safety updates to their regulatory submissions and the handling of the ophthalmic events.
Q. Anything else?

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A. I think that's it.
Q. Okay. If you think of anything else you did, please let me know.
A. I will.
Q.. Now, you said "we," so I want to kind of go through and find out what you personally did and what other people have done, and who those people are. Okay?
A. Uh-huh.
Q. So the first thing you told me was that, "We did a scientific literature review accessing about 3300 articles."
A. Correct.
Q. Did you personally do the literature review?
A. No.
Q. Did you review any of the articles?
A. Yes.
Q. Okay. So who did the initial review?
A. Well, it's done in a series of steps, and I would have to check the assignment records. But one of the research associates would conduct the initial literature search. We have -- we are members of the PubMed system, so we conduct our own PubMed searches at the facility. And the terms that were employed would have been given to him by Dr. Sirois, S-i-r-o-i-s, who is a neuropharmacologist on staff here.

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The initial articles are examined for relevance. We obviously are not interested in articles that are not in English. We may also pare out articles that are abstracts for articles for which we have the full publications. We would delete any articles that didn't seem to be on target as it relates to Viagra or some of the other drugs that were approved later. So the initial cut of the data -- initial cut of the literature would be done by Dr. Sirois.
Following that, the literature is grouped according to the topics of interest. And while there may be some overlap in literature into different topics, we try to break them into the areas of the animal pharmacology, animal toxicology, and then we follow the same review sequence that we use for FDA. We looked at Phase I, if you will, type studies, healthy volunteer-type studies, and then move into the clinical programs. We also look at reports of -- case reports of adverse events, any -- any case series or post-marketing events we can find. If there is not adequate information with the drug of interest, we may look at pharmacologically or mechanistically similar drug products.
I think -- I think that will be about it.
Q. Okay. My question was: Who did the initial review?

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A. The initial review, again, is done by Dr. Sirois, according -- and is grouped according to those topics that I mentioned. And then as I begin the development and writing of the report, I then go to those literature articles and begin reading those articles that are believed to be relevant. And then as I review those relevant articles, I will request which additional articles that I want. Oftentimes there will be articles cited in a bibliography that we may not have picked up, and I will ask for those articles as well.
Q. Okay.
A. So it is a process that goes on over several months.
Q. Okay. But the initial review, which is my question, the initial review was done by Dr. Sirois?
A. Well --
MR. OVERHOLTZ: I'm going to object to form. Asked and answered. What "initial review" means is poorly defined by the questioner. And she has -- the witness has answered the question now twice, in detail, as to what was done.
JUDGE BORG: Dr. Blume, do you understand the question?
THE WITNESS: Yes. I thought I had answered

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them.
JUDGE BORG: Well, do you understand the question?
THE WITNESS: Yes.
JUDGE BORG: Okay. You're able to answer it?
THE WITNESS: Yes. The initial review was done by Dr. Sirois.
MS. LESKIN: Thank you, Doctor..
MR. BECNEL: Let me add an objection. I do not intend to have repetitious questions over and over asked in this deposition. It's a cost. It's not cost effective, and it's costing my clients a lot of money.
JUDGE BORG: Okay. The objection is overruled. It's her time. She gets seven hours.
You can proceed, Ms. Leskin.
MR. BECNEL: It cannot be -- Judge, it cannot be under the federal rules repetitious.
MS. LESKIN: May I proceed?
JUDGE BORG: Yes.
MS. LESKIN: Thank you.
BY MS. LESKIN:
Q. You told me that before Dr. Sirois actually did the review, that there was a research associate who did the PubMed search?

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A. Correct.
Q. Okay. Who was the research associate?
A. I don't know. I would have to check the assignment logs. I don't know.
Q. Okay. How many research associates do you have on staff here?
A. Four.
Q. And what are their backgrounds?
A. Let's see. One of them is -- their undergraduate degree is in, I believe, chemistry; master's degree and their Ph.D. work is in epidemiology.
Another's undergraduate degree had biology and chemistry.
Let's see. A third one's undergraduate degree was in public health, ongoing master's work also in public health.
And the fourth one's undergraduate degree is in business; and graduate program was in information dissemination tools, communication tools.
Q. Now, Dr. Sirois does the initial cut from the articles pulled by one of the research associates. Did I understand that correctly?
A. Well, the way it is conducted is: The PubMed search will provide thousands and thousands of articles that fulfill the terms that were provided by Dr. Sirois,

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and then some of them are automatically struck because of language issues. And Dr. Sirois will then look at the list and make the selection on which of those thousands and thousands of articles will actually be ordered in full format for review.
Q. Okay. What term did Dr. Sirois provide to the research associates?
A. Multiple terms were provided. Of course the name, generic name and brand name, would have been used. The listing of terms relevant to regulatory would be used, such as preclinical, nonclinical evaluations, Phase I, Phase II, Phase III, post-marketing. And those terms are used in conjunction with either Viagra, its generic name. A litany of adverse event terms would be used, adverse medical events. Post-marketing events in general terms are used. And then focusing in on fatalities, we generally start the search with fatality events, and then move to the events of interest.
Q. Do you have a document that lists the research terms that were actually used for the search in this case?
A. I don't, but it would probably be available within the -- Dr. Sirois's records.
MS. LESKIN: We'd request a copy of whatever search terms were used to do the initial review.

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MR. OVERHOLTZ: I would object to that.
MS. LESKIN: We'll follow up.
JUDGE BORG: Overruled.
BY MS. LESKIN:
Q. Do you have --
MR. OVERHOLTZ: As soon as I can get a list of search terms that Pfizer used to look for their adverse events, then we'll start providing a list of search terms.
JUDGE BORG: Is that an objection? Let's stick to the objections, folks.
Go ahead.
BY MS. LESKIN:
Q. Do you have a list of the articles that Dr. Sirois culled from the original search group?
A. Yes. They're on your disk.
Q. They're on the disk that was --
A. Yes.
Q. -- provided to us?
Thank you.
Are they organized by relevance as you've told me that Dr. Sirois did?
A. I doubt it.
Q. Okay. Are the full text of the articles or just the titles provided?

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A. I believe that all the titles are on there, and the text will be in there for those articles which actually were employed in the report.
Q. Did Dr. Sirois provide you with any written summaries of any of these articles or just simply provided you with the articles to review?
A. We may have talked about the articles. There was no written summaries. They were really rather grouped into the categories that I was going to use for evaluation for the report.
Q. Okay. The next thing you identified is that you did an overview of the regulatory events. Who did that overview?
A. Well, the report has a -- the brief overview of the regulatory chronology of the NDA. And I believe -- and again I would have to check the assignment records. I believe the regulatory chronology was prepared by Derek Gutowski.
Q. I'm sorry. Derek?
A. Gutowski, yes.
Q. And what are his qualifications?
A. He is presently in the University of Florida PharmD program. And his undergraduate degree, I think, is chemistry. Might be biology.
Q. Do you know how Derek went about preparing the

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regulatory overview?
A. Yes. The first issue is that we have -- track the FDA database for the NDA number. We also look for regulatory events happening that may be relevant in Europe. We also receive documents -- had received documents from the attorney and had a overview of what regulatory documents we had received. So we included those in a regulatory chronology as well. Then we moved to the various labeling iterations and attempted to track the labeling from its approval until the present..
Q. And is Derek the one who wrote the regulatory overview part of the report for this case?
A. No. I crafted it, but he assembled all of the regulatory documents. And then as I reviewed them, if I needed more, we accessed the additional ones needed.
Q. Now, the next thing you told me is that you did a -- you looked at the regulatory events relating to pharmacovigilance, including any Phase IV work. Who here did that work?
A. Well, we would be tracking Phase IV studies in the literature review that I just discussed, and we would also be looking for any Phase IV studies that may have been reported in the literature, either conducted by Pfizer or conducted by others.
Following that, we would look at the Phase IV

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documents that were provided in the document production, various NDA annual reports, periodic safety update reports, any Phase IV related overviews provided to the regulatory authorities. And then finally we would be examining the FDA database.
MS. LESKIN: Move to --
THE WITNESS: For adverse medical events.
MS. LESKIN: Move to strike; nonresponsive.
BY MS. LESKIN:
Q. My question, Doctor, was: Who here did that work?
MR. OVERHOLTZ: Your question is illogical, because she explained to you, some of it was part of the literature review, some of it was part of another process that she previously described to you. So your question doesn't make sense.
JUDGE BORG: Well, Doctor, are you able to answer the question?
THE WITNESS: Well, I thought I had.
Dr. Sirois assembled what he considered the relevant literature. Mr. Gutowski had reviewed the regulatory -- assembled the regulatory chronology. I believe that Mr. Shearer looked at the studies and assembled the -- attempted to assemble the various labeling iterations employed.

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MR. BECNEL: May it please the Court. The MDL rules call for efficiency, not redundancy. In fact there's admonitions of lawyers for wasting time on repetitious information. I'd like to pull and ask the special master to review the MDL manual that calls for that. Now, this is the second time that we've heard her answer the same question over and over, and that's a violation of the MDL manual for complex litigation.
JUDGE BORG: Then you should go see Judge Magnuson. I've read --
MR. BECNEL: Well --
JUDGE BORG: -- the Court's order -- I've read the Court's order governing the depositions in this case.
All objections are preserved, except as to form and to privilege. Now, that is not a form objection. The deposition is going to proceed. The objection is overruled. Go see Judge Magnuson if you want to, or we can call him.
And, Ms. Leskin, you can proceed.
MR. BECNEL: Well, I would ask the Court, if it has its computer, to pull the manual and read those sections.
JUDGE BORG: I'm reading the Court's order.

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Let's go -- let's go forward, Ms. Leskin.
BY MS. LESKIN:
Q. The next thing you told me was that you -- you asked Mr. Altman to evaluate the AER database, correct?
A. The FDA's adverse event database, yes.
Q. Okay. Did Mr. Altman provide you any written work product from that?
A. I was provided with adverse event counts and a adverse event graphic summary, tabular summary.
Q. Do you have that with you?
A. I believe so.
Q. Okay. Is that on the disk that was provided to us?
A. I don't know. I'd have to check that. But I can get a copy of it.
MS. LESKIN: We would ask for the adverse event counts and tabular summary provided to the witness by Mr. Altman.
MR. OVERHOLTZ: Okay.
BY MS. LESKIN:
Q. Do you know which adverse events were counted for you?
A. Yes.
Q. Which adverse events?
A. I asked Mr. Altman to evaluate the adverse

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event database from the launch of the product, I believe through 2004 or '5 -- I'd have to check that -- and using the same terms that were outlined -- outlined and employed in the public citizen review of the AERS database.

Q. And what terms are those?

A. Just one second. I'll get the adverse event database so I -- there's a complete listing.

Ischemic optic neuropathy. Visual field defects. Blindness. Blindness temporary. Blindness unilateral. Scotoma. Optic nerve infarction. And I think that's it.

Q. Okay. And what document is that that you're reviewing to get the answers to my questions?

A. I'm on page 12 of my report. And this will be on your disk as well. I cite October 20th, 2005 petition that was submitted to the FDA. And included within that petition was an analyses of the FDA's AERS database.. And those terms are listed on page 3 of 8 of the petition.

Q. The information that Mr. Altman provided you, was that any different from the information that summarized in the citizen petition report?

A. Well, it was an amplification of the information in this report.

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Q. In that it went up until the time of his review of that?

A. No. In that I asked him to do it on a yearly basis instead of the cumulative information provided in this petition.

Q. Okay. And he provided that to you in tabular form, you said?

A. Yes, and in a graph.

Q. Okay.

(Telephone interruption.)

THE WITNESS: I'm sorry.

THE VIDEOGRAPHER: We're off the video record.

(There was a discussion off the record.)

THE VIDEOGRAPHER: We are back on the video record.

BY MS. LESKIN:

Q. Other than the adverse events count and tabular graph and summary that Mr. Altman provided to you, did he provide any other information for you?

A. I also asked him to evaluate the AERS database for another drug product.

Q. And what drug product was that?

A. Protonix.

Q. I'm sorry. Which product?

A. Protonix.

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Q. And what is Protonix?

A. Protonix is a drug -- a gastrointestinal drug that inhibits the synthesis of various -- inhibits the synthesis in the stomach of the various acids. And it's used for GERD, reflux, ulcer-type conditions. It's a proton pump blocker..

Q. And what was the purpose of asking Mr. Altman to review the Protonix database for you?

A. Well, I was interested in Protonix because it had ION in its labeling, I believe, as early as 2001. So I was interested in magnitude of reports that Proton -- that had been received for Protonix, since it had added the term quite early in its labeling.

Q. And the labeling you're referring to is the Protonix section on post-marketing reports, correct?

A. I believe I gave you copies of all the labeling in that notebook. And I think it was in their overview of the post-marketing adverse events.

Q. And what did you learn from the review that Mr. Altman gave you for Protonix?

A. Well, I learned it was in their labeling -- I think it was the 2001 labeling -- and that to date, to the present time, I believe they have a total of eight events in the FDA's AERS database. And as I recall, most of those are categorized as nonsuspect.

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Q. Did you look at the adverse events that the -- the ION -- strike that.

Did you look at the ischemic optic neuropathy events for Protonix other than the fact that they had been reported? In other words, did you look at the details of those adverse event reports?

A. Well, his adverse event search was for ionic -- ION. And, no. All I looked at was the number of events that had been received and serious and suspect status.

Q. Do you know whether there is any proposed mechanism for Protonix as to how it could possibly cause ischemic optic neuropathy?

A. I don't know.

Q. Did you do any review to determine whether there was any proposed mechanism for Protonix?

A. I did a brief review, and I did not see a specific mechanism for it. But they had it in their labeling.

Q. Did you review any -- well, do you know when those adverse events have been reported?

A. Yes. There have been, I believe, eight over the entire -- entire approval period for Protonix. I do not recall, sitting here, at what -- how many were in each year. And I know that the term had been added in, at least by the 2001 --

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Q. And how many --
A. -- iteration.
Q. And how many of the adverse event reports had been reported by the time that label update had been made?
A. I -- that's what I said. I don't recall how many were in each year. I was interested in how many -- when I realized that they only had eight total, I'm not as interested in how many each year because they only have a total of eight.
Q. Do you know how many people have taken Protonix?
A. I -- I am not familiar with its annual sales. I know it is among the largest of the proton pump blockers at this time, but I do not know its annual sales, and nor was that really a focus of my interest.
Q. Did you look at any clinical databases for Protonix?
A. I have not at this point, no.
Q. Did you ask Mr. Altman to do any other work for you?
A. No.. I think that -- I think those were the two -- my two interests.
Q. You also mentioned that you did a labeling chronology focusing on the ophthalmic events. Who

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prepared that labeling chronology for you?
A. Well, again I'd have to check the assignment logs. I do not recall who specifically did it. The research associates are all trained in each of these tasks, but --
Q. Would you have records that indicate who did the labeling chronology?
A. Yes.
Q. Do you have records as to how many hours each person on your staff devoted to this case?
A. I'd have to ask our -- our CPA. I don't -- I don't know how their -- how their hours are tallied and then recorded. I don't know.
Q. Well, people who work here are asked to keep track of their time, correct?
A. Yes, of course.
Q. Okay. And you -- and you keep records for that in order to bill --
A. Yes.
Q. -- the plaintiffs' lawyers, correct?
A. Yes.
MS. LESKIN: We would ask for a rundown of all the people who have worked and billed time to this matter from PDG.
BY MS. LESKIN:

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Q. You also said that you -- one other -- the next step you said is, you looked at other labeling for these events from other companies. You've already told me about Protonix. What other companies did you look at or products did you look at?
A. As I recall, we looked at -- we were interested in early inclusions of this term in professional labeling. And I recall we also reviewed Zyvox, the antibiotic Zyvox, and the migraine agent sumatriptan, or Imitrex.
Q. Okay. Zyvox. Why did you look at Zyvox?
A. They have an interesting approach with their post-marketing, as I recall, information. I believe they had ophthalmic events in the -- in the post-marketing section fairly early, I think around 2002. But they handled their post-marketing information by including events based on seriousness -- I believe it's seriousness or number of events or information relating to association and causation. So they -- they describe how they -- how they choose events for their post-marketing. But as I do recall, that antibiotic did have an indication of a retinal event fairly early. I think it was 2002.
Q. What type of ophthalmic events do they have on their labeling?

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A. I'll have to check my labeling notebook for the specific term that they use. I think you have that.
Q. I do.
A. Optic neuropathies, they use..
Q. Do you know how many reports of optic neuropathies have been -- have been reported with Zyvox?
A. If I have the information. I know it isn't in the top group in -- within the FDA's AERS database. If I had the specific number, I don't recall.
Q. Do you know if there's any proposed mechanisms to how Zyvox would cause optic neuropathies?
A. I'd -- well, let me think.
Yeah. I recall an article where they linked -- they -- they don't know, of course, how -- how it causes it, and nor is causation a requirement for their including it in the post-marketing events.
But I recall an article where they looked at the same -- they -- they were look -- trying to see if it was the same apoptotic mechanism that was related to the myelosuppression events. But that's -- that's as much as I remember about it.
My interest was only how firms handled related events during the time frame I was interested in, which was 2000 and forward. And Zyvox handled it by including it because it had a set of criteria they use, which I

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think is a good set of criteria, for when they include events in their post-marketing section. And one of them is not the number of the events but potential seriousness of the event.

Q. And do you know if -- are you aware of any of the regulatory discussions that went on prior to that being added to their labeling?

A. Oh, no, not yet. I haven't been asked to pursue this further, but I may..

Q. Okay. But for this litigation you have not, correct?

A. No. Again, repeating what my interest was, is how did companies handle these related terms and events if they saw them after the product was launched. Did they include it in their labeling? What was the reasoning for including it in their labeling? Were they large contributors to their adverse event database or were they isolated events?

Q. Did you do an analysis of the -- of the Zyvox database, adverse event database?

A. No. I was only interested in the ophthalmic issue and if they put it in their labeling.

Q. Okay. So you didn't look at the overall Zyvox database?

A. No. I haven't been asked to do that yet. No..

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Q. Okay. You also mentioned Imitrex.. What was the reason for looking at Imitrex?

A. I think it was one of the earliest ones that I saw. I think it was '98 or 1999. That Glaxo included it in their labeling.

Q. Do you know how many adverse events they had received before they put it in their labeling?

A. No.

Q. Did you do any type of analysis of the Imitrex adverse event database?

A. Well, I know the grouping of the products that contribute to the ION events in the FDA database. I mean, sumatriptan is not in that group. But other than that, I did not do any more specific work other to -- than to know in 1999 they were adding ophthalmic -- at least by 1999 they had added ophthalmic events.

Q. Okay. So you did not do any analysis of the Imitrex adverse event database?

A. No. I haven't been asked to do that yet.

Q. Okay.

A. And the term that they added, at least by '99, was ischemic optic neuropathy.

Q. Can I just see that again, please?

A. Uh-huh.

Q. Thank you.

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Now, you also said that we, PDG, reviewed company documents that had been provided to you.

Who was responsible for reviewing the Pfizer company documents?

A. Well, it -- there is no one responsibility. It depends on the work that was being done for the various topics that I outlined earlier.

So if a particular person was looking at the labeling chronology, they would also access the Pfizer documents that were provided to us for anything relating to labeling.

The person who was looking at post-marketing events would access the database and look for protocols, final study reports of all of the post-marketing studies that were conducted by the company or in the company's database or documents relating to post-marketing studies.

Whoever was interested in putting together the regulatory chronology outside of labeling would access the database for any documents that might be informative or relating to meetings with FDA, phone calls with FDA, telephone logs, those types of issues.

Q. Your list of reviewed materials that was provided to us with your expert report indicates that you looked at the Pfizer production documents provided

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in hard drive and CD.

A. Yes.

Q. Who provided you those documents?

A. Well, the attorneys provided it to us, but I don't know which office. I can't recall. I'd have to track the records.

Q. Do you know how many documents you were provided?

A. I think it's about -- as I recall, there was around a half a million or 600,000 pages. I think around 34,000, 35,000 documents were on those disks.

Q. Do you know -- well, let me ask you: Was that represented to you to be the entire production that Pfizer made in this case?

A. I don't know.

Q. So you don't know if there's documents that were provided to plaintiffs that were not provided to you?

A. I don't know.

Q. Do you have an index of the documents that were provided to you?

A. I -- I'd have to check. I believe so, but I can't recall.

Q. The materials that were provided to you, were that -- are those on the disk that you gave us this

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morning?
A. Yes.
Q. So that disk contains everything that you reviewed or that the office here reviewed?
A.. Well, the disk includes the documents provided to us, the documents we accessed independently, the literature, labeling iterations. And that doesn't include materials that we have in-house. Obviously I didn't include CFRs and FDA guidances and those types of issues, which would have been -- may have been referenced during the --
Q. Okay.
A. -- review of records.
Q. When you say that you --
MR. OVERHOLTZ: Just to be clear on the record, the disk cannot include the 200 gig hard drive or so of the production, I mean.
MS. LESKIN: Well, that's what I'm trying to find out, is there's two -- there's what we provided to you and there's what was provided to Dr. Blume. And I'm trying to find out how close those two things are.
BY MS. LESKIN:
Q. So were there materials provided to you by the plaintiff that were not included on the disk you

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provided us today?
A. No.
Q. Okay.
MR. ALTMAN: There's some confusion.
BY MS. LESKIN:
Q. Now, you also indicate that on your list of reviewed materials that you reviewed some depositions?
A. Yes.
Q. Now, do you have the page of the reviewed material there in front of you? If not, I can give you a copy.
A. I think that's in that notebook, the small notebook.
Q. Okay. I have another list. I'll give you a copy of that.
What we'll do is, we'll go ahead and mark a copy of your report.
(Exhibit No. 1 was marked for identification.)
BY MS. LESKIN:
Q. Marked as Exhibit 1. And I'll give you a formal copy of your expert report that we received in this case. The last page of that report is entitled "List of Reviewed Materials." Do you see that?
A. Yes.
Q. And on that list, the fifth category -- the --

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I'm sorry, the fourth category are depositions. Do you see that?
A. Yes.
Q. Okay. And it says, "Depositions of Stephen Watt, Stephen Kimmell, Sohan Hayreh, Rachel Sobel, Peter Netland, Peter Ellis, John Gamel, Ian Osterloh, Howard Pomerantz, Gregory Gribko, Gerald McGwin, and Augustine Aruna."
A. Yes.
Q. Do you see that list?
A. Yes.
Q. Do you know who these individual people are?
A. I think so.
Q. Okay. Well, first let me ask you. Above that it says, "Deposition of multiple Pfizer employees, staff, and consultants."
Other than the people listed on the second bullet, what other depositions did you look at?
A. I reviewed depositions that I had from Dr. Hauben, Manfred Hauben.
Q. Anyone else?
A. That's the only one I can remember now but --
Q. Who in Manfred Hauben?
A. He is Pfizer's international pharmacovigilance and safety surveillance.

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Q. And what litigation was that deposition taken in?
A. I think – I believe it was in the Neurontin litigation.
Q. Was there any protective order issued in the Neurontin litigation?
A. Oh, I'd have to check. I don't recall.
Q. Do you know if there's limitations on the use of that deposition outside of the Neurontin litigation?
A. I don't know. I had read it for the Neurontin litigation, and because his opinion on post-marketing surveillance is important, I thought I ought to put a line item in here for him. I did not re-review it for this litigation, but I had reviewed it for the Neurontin litigation.
Q. And does any of the testimony of Manfred Hauben impact your opinion in this case?
A. It could.
Q. Well, I'm not asking if it could. Does it?
A. Well, depending on the question that is asked. Yes. I mean, I agree with what he says about the importance of pharmacovigilance evaluation. So, yes, it would impact what I think.
Q. Okay. Are you relying on his testimony in the Neurontin litigation for your opinion in the Viagra

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litigation?
A. Oh, no. Oh, no.
Q. Are there any other depositions of multiple Pfizer employees, staff, and consultants that you reviewed other than the people listed in the second bullet?
A. Yeah, that's the only one that comes to mind right now. I don't know which ones I had -- was thinking about when I first wrote the report, but I have a list of the other -- I have a list of all of our depositions. So I will look at it. If I'm asked to do that, I will look at it and see if there's any other ones.
Q. Well, did you review anyone -- any other deposition other than the people listed on the second bullet? Did you review any deposition in forming your opinion in this litigation?
A. I don't recall the other ones that I read, sitting here. But I can check the list and let you know.
Q. We'd ask that at a break you check the list and let us know today, please.
What's your understanding of who Stephen Watt is?
A. I don't remember.

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Q. How about Stephen Kimmell?
A. He is a consultant, ophthalmology consultant.
Q. What's your understanding of Dr. Hayreh, Sohan Hayreh?
A. The same. For the -- yes, I believe that Dr. Kimmell provided an opinion to Pfizer, and Dr. Hayreh provided an opinion to the plaintiffs.
Q. Did you review their reports?
A. Oh, yes.
Q. Who is Rachel Sobel?
A. She's an employee of Pfizer. And I recall that she's in the notebooks that I provided to you on periodic safety update-related reports and correspondence.
Q. Who is Peter Netland?
A. I believe he is an outside consultant. And I have his report and his dep -- I have his report and deposition.
Q. And who is your understand -- who -- for whom is he consulting?
A. I think he gave a report indicating no causation, so I think it was for Pfizer.
Q. How about Peter Ellis?
A. I believe he is an employee, as is Gamel and Dr. Osterloh.

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Q. And Howard Pomeranz?
A. Dr. Pomeranz provided the additional -- initial literature relating to the ophthalmic findings. I believe his first publication or presentation was in 1999, and then in 2000, 2005, perhaps 2002.
Q. I'm sorry.. So when you say that he provided the additional literature --
A. Provided the --
Q. -- did he provide it --
MR. BECNEL: The initial.
BY MS. LESKIN:
Q.. -- to you?
A. The initial literature.
MR. BECNEL: The initial. Look.
BY MS. LESKIN:
Q. Okay. Well -- okay.
When he provided the initial literature, he provided that to you?
A. No, to the literature.
Q. Okay. Gregory Gribko?
A. An employee.
Q. Gerald McGwin?
A. Dr. McGwin did the Phase -- one of the studies that are referenced in my report.
Q. And Augustine Aruna?

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A. I also have that opinion. I believe -- I believe Dr. Aruna worked -- provided an opinion for the plaintiffs.
Q. Have you been provided the report or deposition transcript of Dr. Lee, Andrew Lee?
A. Yes, after -- yes. After I wrote the report, I did.
Q. And what's your understanding who Dr. Lee is?
A. I understand -- let me think about Dr.. Lee.
I believe that Dr. Lee's deposition was just recently taken, and he is a practicing -- practicing physician and has consulted with the plaintiffs.
Q. Did you review the report or deposition transcript of Dr. Williams?
A. Which Williams?
Q. John? John Williams.
A. No.
Q. Did you review the report or deposition transcript of Dr. Witt?
A. If I did, I'm not recalling it at this time.
Q. Do you recall the report of Dr. Daniel Shamus?
A. Let's see. I know I cited documents of his in my report with FDA issues, but I don't recall reading a deposition of his.
Q. How about a report provided by him?

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A. Report. I don't recall that.
Q. The plaintiffs haven't provided you a copy of that report?
A. If they did, I'm just not recalling it now. And I don't recall citing it in my report, although I did cite his documents.
Q. Do you know Dr. Simmons Lessell?
A. No.
Q. You haven't seen his report?
A. If I did, I'm not recalling it.
Q. Dr. John Mulcahy?
A. No.
Q. Haven't seen his report?
A. All of these are going to be the same. If I -- if I did have them, I'm not recalling it now.
Q. Okay. Were you provided any briefs or court submissions from this case?
A. I think just the original -- yeah, I think I cited that I had the original, a brief complaint, I guess it was called. I'm not sure what it's called. But I do recall -- I have listed here "plaintiffs complaint," so yes.
Q. Whose complaint?
A. Two names are on it. Let me think. Stanley and Martin. Stanley and Martin.

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Q. Okay. But you weren't provided any briefs that were submitted to the Court?
A. I seem to recollect seeing something that was submitted. I -- it must have been after I wrote the report. I just don't -- I vaguely remember seeing something else; I just don't recall what it is.
Q. Would that be in any of the materials you have here in this room?
A. No.
Q. Do you have any other materials or files for Viagra litigation?
A. I believe that I have a copy of the citizens -- the Stanley and Martin complaint and the other complaint that I saw -- not a complaint. I think it was some filing to the Court. I don't think I spent a lot of time on it, because I can't remember what it is.
Q. At a break, perhaps you can locate that and tell us what it is after the break.
Have you seen any court orders issued by the Court?
A. I received a subpoena for the deposition. That's all I recall.
Q. But nothing -- no order written by the Court or issued by the Court, that you can recall?
A. Relating to what?

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Q. The Viagra litigation.
A. Just -- just the subpoena.
Q. Are you -- you told me that you saw some reports from other experts in the litigation, from this list that we just went through.
A. Yes.
Q. Are you relying on those reports at all in reaching your opinion in this case?
A. Well, I reviewed them, but not -- no.
Q. You're not offering an opinion in this case that Viagra causes NAION; is that right?
A. I haven't been asked to do that, no.
Q. So you're not giving an opinion as to whether or not Viagra can cause NAION?
A. Well, yes, I am not giving that opinion.
Q. Okay. And you are not offering an opinion that Viagra caused Mr. Martin's NAION?
A. Yes, I am not offering that opinion either. Either way, I don't know.
Q. Okay. And you're not offering an opinion that Viagra caused Mr. Stanley's NAION?
A. Again, I haven't been given that information, I haven't been asked to do that, and I am not going to do that.
Q. Okay. When I say "NAION," you understand that

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I'm referring to nonarteritic anterior ischemic optic neuropathy, correct?
A. I do.
Q. Okay. Just easier to say "NAION."
What is NAION? What's your understanding of NAION?
A. My understanding of NAION is that it is the nonarteritic form. And to make it easy, the arteritic form is that form that is generally associated with autoimmune diseases, inflammatory of the giant cells, generally treated with steroid-type therapy.
Nonarteritic ION is an ischemic condition that is not related to the giant cells and leads to a process by which the ciliary bodies supplying the optic nerve are believed to be deprived of the necessary oxygen needed to convert the visual -- the visual signals that we see to the electrical signals that are transferred to the brain for vision.
Q. And what's the basis of that opinion?
A. You want me to -- I've listed the citations, in this report, that I have relied upon. But additionally I've worked with GABA-transaminase inhibitors who are also believed to cause a direct retinal toxicity and lead to similar optic ischemia and a perturbation in a ferrin optic nerve transfer as a result of that oxygen

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loss.
Q.. I'm looking at page 12 of your report, which is where you first talk about NAION, or at least a condition of NAION. Is that where you're referring to?
A. Well, I certainly introduce it there. And then I think if you continue through the report, you will see a listing of references that look at -- that attempted to look at various characteristics of and perhaps mechanisms of, although that was really not a focus of my report.
Q. Right. So my --
A. Page 18.
Q. What on page 18 shows the -- your understanding of what NAION is? I'll make this simpler. My -- I'm just going back to my original question, was: What is the basis of the opinion? And you said that you had citations in the report that you relied on, as well as your other work. So I'm just trying to figure out which citations you're relying on for your understanding of what NAION is.
A. Well, these citations relate to various potential mechanisms that lead to the oxygen deprivation. And that was the question that I was answering.
Q. Okay. Which citation?

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A. Okay. Beginning in 18, we can start, I think the first one that I add is Mahmud's article relating to biphasic hypotensive effect associated with the PDE5 inhibitors. And --
Q. Okay. Let me just stop you there real quick. I see your reference in the first -- top paragraph to Mahmud for the hypotensive effect of Viagra.
A. Okay.
Q. Is that -- am I -- is that the article you're referring to?
A. Yes.
Q. Okay. And is it your testimony that Mahmud refers to NAION?
A. No. He refers to the hypotensive effect.
Q. Okay. I'm -- just now, I really just want to know which articles you're relying on for your understanding of what the condition known as NAION is.
A. You're asking for general textbooks that I may have used for NAION?
Q. I'm asking what the basis of your opinion is. You told me that you had citations in the report. I want to know which citations in the report you're referring to.
A. Well, beginning on page 12, I reference several

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clinical articles that have examined patients with NAION. And I would also offer, as I said earlier, that I did not include textbooks in this report. But I'm quite certain that I also looked at Harrison's Textbook of Medicine. I probably looked at the Martindale review, as well as reviewing these articles, and previous work that I have done with oxygen deprivation of the ciliary bodies relating to the optic nerve.
Q. Okay. So even though you didn't cite Harrison's or the Martindale review, those are materials you relied upon in creating your report, right?
A. Well, they're reference materials that I use in all my work, both work for product development as well as for work with individual drug products.
Q. Okay. Did you use them to create this report?
A. I can't tell you if I went back and relooked at their chapter on ischemic optic neuropathies. I don't know.
Q. Well --
A. I've worked with it in the past, so it probably wasn't necessary for me to go back. But I may have. But I cite, probably, in here 30 or 40 clinical articles that have examined patients with ION or NAION, so I'm sure my knowledge is an accumulation of all of this work.

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Q. What's the background rate of NAION in the general population?
A.. Well, I'm only aware of the, I believe, the two studies that I quote in here. And one is, I believe, 2 in 100,000. And the other one is 10 in 100,000.
Q. And what's the background rate of NAION in men over 60?
A. Oh, I guess it's between 2 and 10. I don't -- I don't know specifically for them. My opinion isn't -- isn't based on the background rate.
Q. Okay. And you don't know what that background rate is for older men, correct?
A. I don't specifically know where in that category they fall, no.
Q. Do you know what the background rate for NAION is in men with cardiovascular disease?
A. I would imagine it's on the higher end of it, but I don't have a specific number.
Q. Okay. And do you know what the background rate is for NAION in men with erectile dysfunction?
A. No. Remember, regulatory opinions, we are directed by FDA that background incidences do not impact the way we handle labeling or information relating to diseases. In fact, we are specifically directed not to consider background incidences. We are looking at an

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adverse event and deciding what to do with it from a regulatory perspective.
MS. LESKIN: Move to strike as nonresponsive.
MR. BECNEL: Objection. How is it nonresponsive?
MS.. LESKIN: There was no question pending.
JUDGE BORG: There was no question to the witness, I believe. Sustained.
MR. BECNEL: Object to the special master's ruling.
MR. OVERHOLTZ: I object as well.
JUDGE BORG: Overruled.
MR. BECNEL: I can put the objection on the record.
JUDGE BORG: Well, I've got to rule on it, don't I?
MS. LESKIN: All objections are preserved.
BY MS. LESKIN:
Q. Now, you have some discussion in your report about the effect of sildenafil on PDE6, right?
A. Yes.
Q. And you understand that PDE6 is a different phosphodiesterase enzyme than PDE5, correct?
A. It's a different iso form of it, yes, I do understand that.

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Q. And the affinity for Viagra on phosphodiesterase type 5 is different than the affinity for Viagra on phosphodiesterase type 6?
A. There is a tenfold difference, one magnitude difference, which in the -- in terms of affinity is -- is a relatively minor difference, a tenfold difference.
Q. Do you know how sildenafil's effect on PDE6 compares to other ED treatments?
A. No..
Q. Now, PDE6 is found in the rods and the cones of the retina, correct?
A. Yes.
Q. And what role does PDE6 play with respect to vision?
A. It is believed in the transfer of the visual to electronic stimuli that it increases -- let me think -- it increases membrane permeability on the outer membrane of the rods and cones.
Q. And what role does PDE6 play with regard to blood flow?
A. PDE6 is a vasodilator which leads to increased blood flow in which increase -- responsible for the increased membrane permeability.
Q. And what's the basis for that?
A. That vasodilators are usually associated with

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increased blood flow.
Q. That PDE6 is a vasodilator?
A. Are you -- are you asking me what in here?
Q. What is your basis for your statement that PDE6 is a vasodilator?
A. PDE6 and PDE5 have similar actions, although a magnitude difference in the binding capacity. My understanding is that both of them lead to vaso -- both of them will trigger a vasodilatation.
Q. Okay. And what is that understanding based on?
A. Okay.
Okay. I cite the work of --
Q. What page?
A. Beginning on page 12. I cite the work of Roth, Hayreh.. I have several studies on page 13 relating to Pfizer-sponsored studies.
Let's see. Who else is sponsoring here?
The work of Mahmud mentions it. Biphasic flow was presented by Hotta in '98. A 2003 review article by Vatansever.
Let's see. I think that's it.
Q. Okay. You said that you -- let's go back to page 12. You said you cite to the work of Dr. Roth. Is it your testimony here today that the work of Dr. Roth establishes that PDE6 is a vasodilator?

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A. No. I recall in one of the reports that he had written, regarding the patients that he had seen early in Germany, that he had noted in one of the patient reports in there, question, "blood flow changes." So that was the first time that I can recall seeing it by someone.
Q. Okay. Which document is that?
JUDGE BORG: Four minutes, Counsel --
MS. LESKIN: Thank you.
JUDGE BORG: -- on the tape.
THE WITNESS: Oh, I don't know which of the specific ones. I have -- I have a whole series of Roth patient reports in the database.
BY MS. LESKIN:
Q. Okay. And is it -- now, you said that it says "blood flow changes"?
A. Question mark, I believe. That's the first time I've seen -- I think that was Roth's work.
Q. Okay.
A. Now, he publish -- did not publish that aside in a separate article. He just notes it in a patient report.
Q. As a possible reason for why that patient had glaucoma, correct?
A. Oh, I don't know if it was one of his glaucoma

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patients or one of the glaucoma patients that also suffered from loss of sight.
Q. Okay.
A. He reports a series. And some have glaucoma alone. And some have sight loss. And some have glaucoma and sight loss recorded.
Q. Okay. And -- and we'll come back to talk about Dr. Roth's patient series.
But is it your testimony that Dr. Roth concluded that the inhibition of PDE6 affected blood flow?
A. No. I was just trying to give you an overview of everything that I put in the report -- everything I recall where blood flow was --
Q. I'm not asking --
A. -- mentioned relating to Viagra.
Q. Okay. I'm not asking about blood flow. You had made the statement that PDE6 is a vasodilator. I want your citation for your support for that statement.
A. Well, I -- PDE6 leads to -- can lead to vasodilatation, yeah.
Q. Okay. I want the support for that statement.
A. I gave it to you.
Q. You're telling me that Dr. Roth's question mark about blood flow is support for your conclusion that

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PDE6 is a vasodilator?
A. No. I was just trying to be complete and answer everywhere in the port -- report where that was addressed. And I recall in his patient series that he had made that notation.
MS. LESKIN: Okay. We need to change the tape, so let's go off the record.
THE VIDEOGRAPHER: We're off the video record.
JUDGE BORG: Let's take five minutes.
(Recess from 10:35 a.m. until 10:54 a.m.)
THE VIDEOGRAPHER: We are back on the video record.
BY MS. LESKIN:
Q. I just want to go back, Doctor.
Right before the break, I had asked you the question: "What role does PDE6 play with regard to blood flow?"
And you answered: "PDE6 is a vasodilator which leads to increased blood flow."
A. Right. I thought about that when I left, and I think I was talking too quickly. Let me clarify.
Q. Okay. Well, let me ask you a question again.
What role does PDE6 play with regard to blood flow?
A. It's the inhibition of -- let me -- let me

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answer that by going backwards a little bit.
PDE5 first. PDE5 inhibition of the phosphodiesterase activity leads to an accumulation of what we'll just abbreviate as GMP. And GMP leads to vasodilatation. We have no idea all of the places where phosphodiesterase-5 or its inhibition may be impacted in the body, but we certainly know it leads to an overall systemic lowering of the blood pressure.
We know that PDE6 is in other areas of the body. We know that it is in the rods and cones of the retinal cells, and that inhibition of PDE6 just in the rods and cones area are believed to affect, as I noted earlier, increased membrane permeability, maybe some perturbation in the apoptotic cycle, and may be responsible for the blue-green tinge that we hear about with -- with various agents, including the erectile dysfunction drugs.
As it relates to phospho -- inhibition of phosphodiesterase, phosphodiesterase is responsible for degrading and removing GMP levels. So inhibition of phosphodiesterase inhibits, if you will, the inhibition, so you have an increase in the -- the activity of GMP.
Now, as it relates to the blood flow, your question, the blood flow in the eye, I don't know if anyone is exactly sure how the blood flow is influenced.

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Is it a result of a direct action in the eye or is it a result of the fact that there is a systemic lowering of blood pressure; that lowering of blood pressure is bodywide, systemwide, leads to lowering of blood pressure, leads to vasodilatation? We see it systemically. We see it, also, within the eye.
So I hope that clarifies what I was saying before the break.
Q. So is it your testimony that the inhibition of PDE6 has an ultimate effect on blood flow?
A. I don't know if that's the case or if it is the systemic effect. I think -- I know that it has an effect on PDE5, and that leads to an increase in the blood flow in many areas, I mean in -- well, certainly in the lung, with the erectile dysfunction actions. And it translates, also, to increased blood flow in the eye.
Q. Okay.
A. But the inhibition of the PDE6 in the rods and cones is a separate action, and that may well be -- underlie the effects on the perceived observations of blues and greens.
Q. Do you have any support for a conclusion that the inhibition of PDE6 has an effect on blood flow?
MR. OVERHOLTZ: Object to form; asked and answered.

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JUDGE BORG: Tell me where in the form.
MR. OVERHOLTZ: I believe that she just said that -- she said she didn't know whether PDE6 -- inhibition of PDE6 had an effect on blood flow or that it was the PDE5. And then she --
JUDGE BORG: And the question?
MS. LESKIN: Do you have any support for a conclusion that the inhibition of PDE6 has an effect on blood flow?
MR. OVERHOLTZ: So my -- my -- my objection is, there's a lack of foundation that there is such a conclusion that there's an effect of PDE6.
JUDGE BORG: Dr. Blume, do you understand it? Are you able to answer that question?
THE WITNESS: I'm not exactly sure that I understand --
JUDGE BORG: Okay.
THE WITNESS: -- what this question is and how it differs from what I just answered.
JUDGE BORG: Well, I appreciate that. But do you understand the question?
THE WITNESS: Yes, I think so.
JUDGE BORG: Okay. Okay. And you're able to answer it?
THE WITNESS: Well, yes, with -- but my answer

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is: I -- I don't know if inhibition of PDE6 also causes that. I don't know if anyone knows that. But my interpretation of its effects -- of the effects of the erectile dysfunction drugs in the eye are independent of that.
BY MS. LESKIN:
Q. Are you aware of any evidence that Viagra's effect on PDE6 is related to NAION?
A. Viagra inhibits PDE6, and PDE6 is --
Q. Are you aware --
A. -- my understanding is, its actions in the rods and cones are more associated with the perceived color changes.
Q. Are you -- is it your opinion that an inhibition of PDE6 can cause NAION?
A. I don't know. I don't know if anybody knows that. I don't know.
Q. And you're not offering that opinion today, correct?
A. I don't know. I believe that Viagra's effects on NAION are independent of that action, but I don't know if PDE6 also has some function on blood flow within the eye.
Q. Are you aware of anyone who has put forth the theory that Viagra's effect on PDE6 causes NAION?

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A. I don't know of that. I don't think we know enough about the distribution of PDE6 outside the rods and cones to answer that.
Q. I -- that's -- I just want to answer my -- my question is very different than that, I think.
Are you aware of anyone who has put forth the theory that the effect of -- on PDE6 is what causes NAION?
A. I am not aware of that.
Q. Would studying the effect of Viagra on PDE6 -- well, strike that.
Do you know what glaucoma is?
A. Increase in intraocular pressure.
Q. And what's the basis for that?
A. That I know that answer?
Q. Yes.
A. I just -- I don't know. I mean, I've known it for years. I've worked with beta blockers.
Q. Is it your opinion that glaucoma is related to NAION?
A. In the etiology of NAION?
Q. Yes.
A. No, I don't believe that I've said that. I know that intraocular pressure can impact distribution of blood flow; so I guess indirectly it could be

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involved in the flow -- blood -- in blood flow within the eye. But I haven't specifically connected.
Q. And are you aware of anyone who has put forth the theory that glaucoma is causally related to NAION?
A. That glaucoma causes NAION?
Q. Correct.
A. I recall a discussion in one of the expert's report about the impact of intraocular pressure in blood flow. But other than that, I don't remember anything else.
Q. Would a study of the incidence of glaucoma provide any insight on the incidence of NAION?
A. I don't know. I don't know.
Q. Do you know what third nerve palsy is?
A. No.
Q. Is it -- do you have an opinion as to whether third nerve palsy is related to NAION?
A. No.
Q. Are you aware of any study demonstrating that third nerve palsy is related to NAION?
A. No.
Q. Do you know what retinitis pigmentosa is?
A. I recall that it's in the labeling. I think -- it's in the labeling of several drug products. But -- but I'm not -- I'm not familiar with them.

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Q. Do you know whether retinitis pigmentosa is related to NAION?
A. No.
Q. Are you aware of anyone who says that retinitis pigmentosa causes NAION?
A. No. I just recall seeing it as an exclusion criteria in some of the ophthalmic studies.
MR. OVERHOLTZ: Lori, this is such a waste of the Court's time, our time, everybody's time. We have never ever come into this court, none of our expert report, none of our testimony, none of our depositions have ever attempted to link any of the issues that you're going over now, out of your little outline that somebody's prepared for you, that any of these conditions are related to NAION. Can't we keep this deposition limited to the topics in her report so we can get through this? This is a complete waste of time.
JUDGE BORG: The objection I think I understand is overruled. Let's proceed.
BY MS. LESKIN:
Q. Do you know what diabetic retinopathy is?
MR. OVERHOLTZ: Judge, I have to restate this objection. This expert has not offered any opinions related to these issues she's questioned about;

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neither have any of our other experts. This is just a waste of her time.. I don't -- setting up some -- I don't know even know what it's about, if it's setting up some kind of defense in some other case they have pending, but this expert is not here for these issues.
If someone else -- if somebody else has sued Pfizer and claims that because it can cause retina -- is contraindicated in the people with retinitis pigmentosa, that that's how it causes NAION, then go take the depositions of their experts about those issues. But wasting our expert's time, our time, your time, all on the clock while they bill and ching, ching, ching, while our clients suffer with blindness, is just an unbelievable affront, and it's -- it's unbearable. It's unbearable what we've said.
They've now spent more time deposing our witnesses in this litigation than we have spent deposing Pfizer. It's ridiculous. This massive corporation has hundreds of employees working on this drug. They've now deposed more people, more times, more hours than we've deposed them.
MR. BECNEL: I need to put for the record that this MDL is out of control financially in terms of

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the method of Pfizer doing discovery and the irrelevant nature of their questioning concerning every issue dealing with every other piece of litigation Pfizer is involved with, and that that's improper. It violates the rules of the MDL manual on complex litigation. And it's continued throughout the course of this supposedly, quote/unquote, discovery, and that is not appropriate; and, therefore, you leave me no alternative but to file a complaint dealing with these issues. And I will so file.
MS. LESKIN: Go for it.
MR. BECNEL: I always do.
JUDGE BORG: Your objections are noted for the record. They are overruled. I'm following the Court's order regarding depositions. If you wish a protective order or some other guidelines from the Court, then I think you need to get them from the Court.
MR. OVERHOLTZ: Okay. Just let me say that that's fine. I understand your ruling. If questions continue today outside of the scope of her report, outside the scope of the opinions that she has given, I'm going to file a motion for protective order and end the deposition. I just want to put

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counsel on notice of that.
MS. LESKIN: Can -- you know what? Can we go outside of the presence of the witness? And I will make a proffer so that we can stop this interruption and I can proceed with my deposition in an efficient manner.
JUDGE BORG: Well, let -- do you want to do that right now --
MS. LESKIN: Yes.
JUDGE BORG: -- or do you want to proceed with the deposition?
MS. LESKIN: No. I want to do that right now, because I want to stop being interrupted after every other question.
JUDGE BORG: All right.
Dr. Blume, would you mind excusing us here, please?
THE WITNESS: No, of course not.
(Dr. Blume exited the proceedings.)
MR. BECNEL: It is the most amazing thing I've ever heard of for Ms. Leskin to say she wants to stop objections. In the deposition of Dr. Hayreh, every other question was objected to. Every other question.
JUDGE BORG: Okay. It's Ms. Leskin's turn to

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respond to your -- both of your objections.
MS. LESKIN: I will start on page 12 of her report. "Soon after product launch, Pfizer quickly became aware of additional ophthalmic adverse events associated with Viagra from a variety of sources."
She then goes on to cite Dr. Watt's "Adverse Event Reports on Glaucoma."
She continues later on, on page 18 -- 16, "Pfizer was also aware of reports of a number of other ophthalmic adverse events, including NAION."
And she cites, at the bottom of the page, "Additional adverse ophthalmologic events in association with sildenafil have been published in the medical literature," including Donahue, which is a third nerve palsy case; Vobig, which refers to ERG changes; Burton, which is diabetic retinopathy; Murata, which is a Japanese case involving central serous chorioretinopathy, which is a retinal detachment; Tripathi and O'Donnell, which is branch retinal artery occlusion; Gabrieli, which is visual halos; Luu, which is ERG effects; Balacco, which is ERG effects.
(Reporter clarification.)
MS. LESKIN: Luu, ERG effects. Balacco, B-a-l-a-c-c-o, ERG changes. Bertolucci, which is a

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hemi-retinal artery occlusion due to sex. Allibhai, A-l-l-i-b-h-a-i, another central serous chorioretinopathy. Jagle, again looking at the ERG differences. Marsh, retinopathy of prematurity. Quiram, serous macular detachment.
And she goes on. She refers to other adverse event reports throughout. She talks about exposure of --
MR. OVERHOLTZ: Talking about things --
MS. LESKIN: Hold on.
MR. OVERHOLTZ: It's a pretty long proffer. Okay?
MS. LESKIN: Okay. Well, let me finish my proffer. You had hours and --
JUDGE BORG: Okay. Finish.
MR. BECNEL: What hours have we had?
JUDGE BORG: Wait, wait, wait. Whoa. Stop it.
MR. BECNEL: Wait. I want to know what hours have we had. It's an out-and-out lie.
JUDGE BORG: You don't get to ask the question at the moment.
Ms. Leskin, finish with your proffer.
MS. LESKIN: She continues to say, on page 19, "The continued accumulation of serious adverse ophthalmologic events associated with Viagra use and

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found in the medical literature should have prompted Pfizer to undertake a more thorough analysis of NAION-related events associated with the drug."
So if she's going to rewrite her report to remove any reference to an event other than NAION, I won't ask about events other than NAION. But she is relying on all of these adverse events in the database and in the literature on things other than NAION, and I should be entitled to set up my motion to exclude any reference to those adverse events by getting her to acknowledge that they are not related.
JUDGE BORG: Mr. Overholtz.
MR. OVERHOLTZ: Your argument is 100 percent completely illogical, and your questions were not in any way directed towards whether or not Ms. -- Dr. Blume had any opinions as to whether or not -- not one of your proffers says that Dr. Blume has an opinion as to whether retinosa or any of those things are related to NAION.
You obviously don't understand her report, or either you're feigning here just so you can create a record of some -- so you can make up issues to take to the Court's attention. But the providing background information about adverse events that

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Pfizer has had from an ophthalmic nature is not her opinions in this case.
And she has not given an opinion that Viagra -- that retinosa -- retinosa pigmentosa causes NAION, and neither does any of the statements you said make such conclusions. It says Pfizer's received those adverse event reports. And those are all true, factual statements, background. Okay?
If you want to start out by asking her a deposition of expert like other lawyers do it, which is, "Dr. Blume, do you have an opinion in this case, okay, tell me what it is, now let me ask you what the basis of that opinion is," that would be the way to do this deposition. But to sit there and ask about things that she hasn't given opinions about is a complete waste of time.
MS. LESKIN: And just to conclude, on page 41, under her conclusions, "An association between use of Viagra and a number of serious and even irreversible ophthalmologic-related events was apparent even prior to its regulatory approval."
And I think everyone will agree that there is no report of NAION prior to approval.
"Evidence can be found in the growing collection of both internal and public documents

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discussing the occurrence of adverse events such as blindness, ischemic optic neuropathy, nonarteritic ischemic optic neuropathy, retinopathy, glaucoma, and many others. Despite an accumulating knowledge of potentially serious ophthalmologic adverse events, Pfizer avoided timely updates to the Viagra product line label, thereby exposing users to unnecessary and unknown events. This is especially concerning because a significant percentage of the patient population receiving Viagra possesses one or more risk factors which may predispose them to NAION and related events. Although Pfizer did update the Viagra product label in July 2005, this change does not adequately reflect the number and severity of the serious ophthalmologic events associated with the drug over three years later."

MR. OVERHOLTZ: The problem is --

MS. LESKIN: So that part is not limited to NAION.

MR. OVERHOLTZ: The problem is, your questions are geared towards causation.

MR. ALTMAN: That's --

MR. OVERHOLTZ: And they're not geared towards liability. The fact that Pfizer had all of these reports did put them on a duty to look into the

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ophthalmic issues more. If you want to ask about that opinion that Dr. Blume has given, I think that's fine. But asking her causation questions, which she has not been presented as a causation witness here, is waste of this Court's time.

MS. LESKIN: Well, I think I'm absolutely entitled to ask her her knowledge of the -- of the events and whether she's saying that it's at all related to NAION.

JUDGE BORG: Well, she's --

MR. OVERHOLTZ: She never said it's related to NAION.

JUDGE BORG: She has also testified that she hasn't been asked to be given -- to give certain opinions, and she's disqualified herself on those by virtue of the answer.

Listen, folks, here is the deal. We've got a witness here, and the reason that we're here is to get it done. I understand your objections, Mr. Overholtz, and I'm not going to -- and I'm not going to say whether or not they ought to be granted or not. You can take that up with the Court.

But the fact of the matter is, nobody wants to come back here and do this again --

MR. OVERHOLTZ: No.

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JUDGE BORG: -- if the Court concludes that -- that Ms. Leskin go -- can go where she wants to go. So we're going to get it done. We're going to get it on the record.

All of your objections are preserved, whether or not you state them, but for, of course, the form, privilege, and responsiveness.

So you're on the record with this. You know, have at it with the Court when the time comes. But we've got to get this done.

MR. BECNEL: But, Judge Borg, the problem is: The purpose of the plaintiffs and the defendants paying you to come down here is not to tell us we got to go to the Court. You've got to make calls.

You know, I've never been in an MDL other than in Minnesota twice, in the whole country. And I've been doing these for almost 40 years.

Well, we have a special master of discovery that's -- that rides herd on us here.

And the problem is, in almost every other MDL, we stop, we call the Court or the magistrate judge, and they make a ruling right there based upon the evidence we've given them, every one I've been involved in over the years.

But we have you here now. And you tell us,

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well, we've got to go back to the judge. That makes no economic sense whatsoever; because that doesn't deal with efficiency, that doesn't deal with whether we got to come back here or not come back here. We've got stay here no matter what.

And the purpose of your being here should be to make these calls. The purpose of you being here shouldn't be for me to say, "The Manual for Complex Litigation requires us to follow these rules, and if you do things that are repetitious, you get penalized for that."

It's not just because you got seven hours, you waste seven hours or you use seven hours. If it's relevant, certainly. And many times, seven hours might not be enough in a case. And we could say, "Judge Borg, we haven't covered all of the issues. Can we go on over that?" That's your role, as I understand, as special master.

We don't have any choice in the picking of a special master. And as I said, I've never had a special master ever that does what you're doing. But when we got you, we ought to be able to have some resolution in some of these issues. We ought to not be able to be told, "Well, go back to the judge." That makes no sense.

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And -- and the manual says that. It's not me saying it. It's people who created the manual, not me.

JUDGE BORG: Well, I'm reading the Court's order, which governs this case. So the objections are noted. They're overruled, and we're going to proceed with the deposition.

(There was a discussion off the record.)

(Dr. Blume re-enters the proceedings.)

MS. LESKIN: You didn't go off.

THE VIDEOGRAPHER: Correct. We were not off the video record.

BY MS. LESKIN:

Q. Dr. Blume, do you have an understanding what diabetic retinopathy is?

A. Other than prolonged diabetes associated with decreased retinal function.

Q. Do you -- do you believe -- well, strike that.

Is it your opinion that diabetic retinopathy is related to NAION?

A. I don't know.

Q. Are you aware of anyone who has put forth the opinion that diabetic retinopathy is related to NAION?

A. I'm not aware either way.

Q. Would a study of diabetic retinopathy provide

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any insight as to the incident rate of NAION?

A. Well, I mean, all studies yield information that might be useful. But, I mean, I guess if there was a, you know, a large study done that looked at age controls across time, and enough data were collected that one could look at -- look at these, yeah, I guess it could be helpful, if someone did a big enough study..

Q. Would -- if you wanted to determine the incidence of NAION, would you study -- would you focus your study on diabetic retinopathy?

A. Oh, I don't know. I don't know how to answer that.

Q. Okay. Do you know what retinal detachment is?

A. Yes.

Q. What is retinal detachment?

A. My understanding is that the retina literally physically detaches from the anchoring membranes and is then no longer able to funnel the visual stimuli to the optic nerve for transfer to the brain.

Q. Is that the same thing as chorioretinopathy?

A. I don't know.

Q. Is it your opinion that retinal detachment is related to NAION?

A. Oh, I've never heard that, but I've also not studied it.

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Q. And you're not aware of anyone who's put forth the opinion that retinal detachment is related to NAION?

A. I haven't researched it. I don't know the answer either way.

Q. Do you know what retinal artery occlusion is?

A. No.

Q. Do you know whether retinal artery occlusion is related to NAION?

A. No. I don't know what it is.

Q. Do you know what retinopathy of prematurity is?

A. Retinopathy of prematurity?

Q. Yes.

A. No.

Q. And do you have any opinion as to whether retinopathy of prematurity is related to NAION?

A. No. I don't know what it is.

Q. Do you know what macular detachment is?

A. Macular detachment?

Q. Yes.

A. No.

Q. Do you have any opinion as to whether macular detachment is related to NAION?

A. I -- I don't know either way.

Q. Are you familiar with the term "safety signal"?

A. The safety signal?

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Q. Yes.

A. Uh-huh.

Q. Would you agree to me that the safety -- would you agree with me that a safety signal is a concern about an excess of adverse events compared to what would be expected with a product's use?

A. Could you repeat that?

Q. Sure. Would you agree with me that a safety signal is a concern about an excess of adverse events compared to what would be expected to be associated with a product's use?

A. Well, my understanding of a safety signal is any issue that you observe with your data that makes you think differently. And it can include a new event or some change in the frequency or magnitude of a previous event. I generally do not qualify whether something is a signal or not based on what I would anticipate to see in a given population, simply because we are instructed to not do that.

Q. Okay. Well, let me give you what we've marked as Exhibit 2.

(Exhibit No. 2 was marked for identification.)

MS. LESKIN: I have a copy for counsel.

BY MS. LESKIN:

Q. This is the March 2005, Guidance for Industry,

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Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment, from the FDA, right?
A. Yes.
Q. And you cite this in your report, correct?
A. Yes.
Q. Turn with me to page 4. And in the second paragraph it says, "In this guidance document, 'safety signal' refers to a concern about an excess of adverse events compared to what would be expected to be associated with a product's use."
A. Yes.
Q. Do you see where I read that?
A. Yes.
Q. And that's how the FDA is defining that, correct?
A. Well, yes, but that's only part of the study. You have to continue with the guidance and FDA notes in this guidance that one cannot limit the importance of a safety signal based on post-marketing information because of the absence of complete post-marketing information. So one cannot rule out a signal based simply on comparison to what would -- what is a baseline incidence or what one would anticipate in that population; because we know that only 1 to 10 percent of all adverse events are ever reported.

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Q. Okay. And we'll come back to that.
But as the FDA writes in this document, they're referring to a safety signal as an excess of adverse events compared to what would be expected to be associated with a product's use, right?
A. Yes, you read that correctly.
Q. Okay. Now, a safety signal is not the same as causation, right?
A. Of course.
Q. Okay. And a single case report isn't necessarily a safety signal, right?
A. Can be, but it might not be.
Q. Okay.
A. Depends on the situation and the data.
Q. And depends on the type of event?
A. Yes. One cannot rule out that it's a signal simply because it's -- you have one or two events. But because you have one or two events may not be a signal. Depends on the data.
Q. And when you get a safety signal, the obligation of a pharmaceutical company is to investigate that safety signal, correct?
A. Yes.
Q.. And sometimes that safety signal may turn out to signal a cause and effect relationship, but sometimes

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it might not, correct?
A. I'm sorry. Sometimes a safety signal may lead to a cause and effect assessment?
Q. Sometimes it may turn out that the safety signal signaled a cause and effect relationship, but sometimes it may not be a cause and effect relationship, right?
A. Well, there's very few ways in which you can address causation. The only way I can imagine that a safety signal would address causation is if it were evidence of a rechallenge event.
Q. Okay. My question, I think, may have been unclear.
You told -- we agreed that when you get a safety signal and identify something as a safety signal, there's an obligation to investigate it, right?
A. Of course.
Q. And that investigation may lead someone to determine that there is in fact a cause and effect relationship, right?
A. I don't -- I guess it could. I mean, it's not really -- I mean I -- yes, I guess if one saw a safety signal, your client or companies could design studies designed to address causation.. I mean, it's sort of two different issues.

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Q. Okay. They also could do some investigation to find out that it's simply coincidence, right, that there is no cause and effect relationship?
A. Well, cause -- causality can only be established in really three ways. And if they did an evaluation, and one of the -- and they ruled it out, I guess it's possible. But that generally isn't what we do in industry with a -- with a safety signal.
Q. Okay. Well, let me direct you back to that same paragraph on page 4 of Exhibit 2 that we were just looking. At if you look at the next to last sentence, the FDA writes, "Signals generally indicate the need for further investigation, which may or may not lead to the conclusion that the product caused the event," right?
A. You may find out that caused or didn't cause the event. That -- okay. But that doesn't impact what we do with the signal.
Q. Okay. Now, you're not saying in this case that immediately upon receiving a safety signal, there's an obligation to change your label, are you?
A. Well, it depends on the circumstances. For every -- I mean, there are labelings that have been changed when there have been two events noted in the AERS database, and labeling has been changed immediately. And it's noted that they don't have proof

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of causation, but it's been observed, hasn't been in the labeling, so we're putting it in the labeling. So I think that companies have changed labeling with very small-number events and no evidence of causation. And we are encouraged to do that and permitted to do that.

If you're talking about this particular case --

Q. No. I'm --

A. -- Viagra --

Q. I'm talking in general.

A. Okay. In general I think companies look at their data, and even with few events, depending on the seriousness of the event or other factors, may or may not change labeling for -- for various reasons. But you certainly don't rule out changing labeling when there's been one or two events.

Q. Okay. But is it the obligation of a company to change its label based solely on one or two events?

A. I think it's the obligation of the company to make sure that important information is in their labeling. It is the -- that responsibility rests with the company. And I can't answer it for all times. I mean, in this report I noted a Dear Doctor letter, a labeling change that I made based on two adverse events noted in the AERS database. So it is done with one and two. Product development programs are stopped with one

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or two events.

So, yes, I think depending on the frequency of the event, the seriousness of the event, what information you have with the event, it is incumbent upon a company to consider a label change even with very few numbers of events.

Q. You -- you just raised something that you have in your document here. You have on page 9 of your report where you said, "There are examples of labeling changes and Dear Doctor -- Dear Healthcare Professional letters based upon manufacturer's receipt of only two or three events."

Is that what you were just referring to when you testified about that? You said you said in your report that you --

A. I think so.

Q. Okay.

A. Yeah.

Q. What are the examples that you're referring to in this report?

A. Well, the one that I have given is my own Dear Doctor letter where I sent out a Dear Doctor letter and made a labeling change when we received two reports of dose-related hypertension change with elder -- for elderly and Parkinson patients. And that's -- that's

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the one that I'm using.

Q. Okay. That's -- nothing cited in this report for that, though, right?

A. Oh, I've used it so many times. Yes. But that's one that I'm using.

Q. Okay.

A. And it's currently on the FDA website, so it's readily available.

Q. Now, one thing a company can do to investigate a safety signal is to go back and look at their clinical database, right?

A. Well, they -- that's one of the things they should do.

Q. Yeah. And that's a reasonable response, to go back and examine the clinical database?

A. It is. The -- the worlds are so different between the patients that are in a clinical trial and what happens once the product gets in the real world. Of course it's always interesting to go back and look, but it is certainly different populations that you're looking at. And that's why post-marketing information is so critical to the company, is because that is the picture of the real-world use of the product, not the rather artificial populations that we use in our clinical trials.

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Q. Okay. So one response to a safety signal would be to go back and look at the clinical database?

A.. Yeah, you could.

Q. And another response would be to go back and look at any animal testing that had been done, right?

A. Yeah, you could.

Q. And to -- another response would be to review the literature, correct?

A. Well, companies always ongoing reviewing literature. But of course.

Q. And another response could be to evaluate whether there is any plausible biological mechanism for the event that's being identified?

A. Right. You could look at that.

Q. And one thing that would be reasonable to do would be to evaluate the background rate of the event in the population being treated?

A. Well, not so much. I don't -- I don't agree with that. It's interesting, but if you're looking at a post-marketing adverse event and you know that you're only going to receive 1 percent of all of the people who report that event, it's interesting to look at the background incidence, but it's impossible to compare the two. So one cannot rule out the importance of event based on a perceived background incidence in the

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population because you simply can't compare the two numbers.
Q.. But it is important to put the event into context, isn't it?
MR. OVERHOLTZ: Object to form; lack of foundation.
JUDGE BORG: How -- where? How so?
MR. OVERHOLTZ: It's important to put the event into context? I don't even know what that means: context. What is she referring to, what type of context?
JUDGE BORG: Ms. Leskin, you want to expand on that?
Sustained. I don't know what that means either.
BY MS. LESKIN:
Q. Did -- one thing a company could do when it has a safety signal is to consult with experts in the area?
A. Yes.
Q. And get their view as to whether this represents a true signal?
A. Well, a signal is defined as if it makes you -- if it's a new event or makes you look differently on something you saw in the past. I'm not sure what the definition of a true signal is.

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Q. Okay.
A. Signal is simply anything that makes you look differently, something new or some change in something, a magnitude of frequency you've seen before. I think it's important to consult outside experts, of course, but I don't know if they really can address whether something is a true signal.
Q. Okay. They could help you put the -- help you better understand the event being reported?
A. I guess if it's a particularly difficult event to understand, I guess they could be helpful.
Q. I want to talk a little bit more specifically about Viagra.
Now, you're aware that the company, that Pfizer, submitted a new drug application to the Food & Drug Administration for Viagra, correct?
A. Yes. I have that cited in my report.
Q. Okay. And did you have the opportunity to review the NDA for Viagra?
A. I did review parts of it, yes.
Q. Okay. Which parts of it?
A. I looked at the, primarily, at the medical. I did scan over the animal review.
Q. Okay.
A. And I did look at the pharmacokinetic data.

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Q. Before submitting -- before submitting the NDA, are you aware that Pfizer submitted an IND?
A. I believe they did. I don't know if I quoted the IND, though. I believe they did.
Q. That's an investigation of a new drug, correct, a new drug application, correct?
A. Yeah, a request for exemption, yes.
Q. Do you know when that -- an IND was filed?
A. No..
Q. Do you know what data was included in the IND?
A. No.
MR. BECNEL: Excuse me, Ms. Leskin. Are you going to make this a part of the deposition or not?
MS. LESKIN: Yeah. We marked that as Exhibit 2.
MR. BECNEL: 2. Okay.
BY MS. LESKIN:
Q. Did you have the opportunity to review the IND in this case?
A. No.
MS. LESKIN: I'm going to mark as Exhibit 3, this is an excerpt from the new drug application. It's Bates stamped 002000947 through 950.
(Exhibit No. 3 was marked for identification.)
BY MS. LESKIN:

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Q. Have you seen these pages before?
A. I may have. But can you put these in the context for me? I don't -- page 6 of what?
Q. This is a section of the NDA, I believe part of the initial summary, I believe. And the section that I've given you, just for the record, is Section H.2.B, entitled "Interactions With FDA."
MR. OVERHOLTZ: I'm going to object to the document. I'm trying to look for anywhere on here that indicates what it is and where it comes from. I don't know if this is Pfizer's summary of what has happened or what this is.
JUDGE BORG: Ms. Leskin.
MS. LESKIN: I'm trying to get the context here.
BY MS. LESKIN:
Q. Okay. To help you out, I'm going to mark as Exhibit 4, a document that's entitled Index to Sildenafil NDA.
(Exhibit No. 4 was marked for identification.)
BY MS. LESKIN:
Q. I'll represent to you, this is the index to the NDA that was filed with the Food and Drug Administration, Bates stamped 002000001 through 46. Have you seen this index before?

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A. I may have. I don't recall it, though.
Q. Okay. And --
MR. BECNEL: It says "redacted" on it. What is redacted?
MS. LESKIN: Pursuant to the protective order and the objections that were made at the time of production, it's the CMC section. The chemistry manufacturing section has been redacted.
MR. ALTMAN: I'm completely confused. You were asking her about the IND, and then this is out of the NDA. Are you totally off the IND topic?
MS. LESKIN: No, we're not. I'll -- don't worry. We'll get there.
BY MS. LESKIN:
Q. If you look at page little 7.
JUDGE BORG: Well, let's get this document identified again. I don't know that that's that clear.
MS. LESKIN: Okay. This will be --
MR. OVERHOLTZ: I don't even which document we're trying to do.
MS. LESKIN: -- Exhibit 4, which I've marked, is the index to the NDA.
BY MS. LESKIN:
Q. Have you seen the index before, Doctor?

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A. As I -- I just answered that. I may have; I just don't recall it.
Q. Okay. If you look at page little 7, Roman numeral VII on the bottom. It's Bates stamped 002, and then lots of zeros and a seven.
MR. OVERHOLTZ: I don't know if this is a final or a draft.
MS. LESKIN: This is the final as produced in this litigation.
THE WITNESS: All right.
BY MS. LESKIN:
Q. Okay. And you'll see there's a -- it says "2, Overview of Clinical Studies"?
A. Yes.
Q. Okay. And you go down to B., where it says "Interactions With FDA"?
A. Yes.
Q. Okay. And you'll see that says page 949, all the way on the right where it says under "page number"?
A. Yes.
Q. Okay. And if you go back to what we marked as Exhibit 3, you'll see this has a "949" on the bottom?
A. Yes.
Q. Okay. So that's the section of the NDA that this comes from. Okay?

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So have you reviewed this section of the NDA entitled "Interactions With FDA" before?
A. I -- I don't recall if I did or not, when I reviewed it.
Q. Were you aware that representatives of Pfizer had met with the FDA before they filed the NDA?
A. Of course. That's required.
Q. Okay. And you'll see the first line under H.2.B, "Interactions With FDA," says, "The original IND for sildenafil was submitted on December 7, 1994"?
A. Yes.
Q. And that "On January 9, 1995, Pfizer was informed by the medical reviewer, that clinical trials under IND No. 46,863 could begin"?
A. Yes, I see it.
Q. Okay. Had you read that before?
A. Oh. If I did, I just don't recall it.
Q. Okay. So does this refresh your recollection that Pfizer did in fact file an IND in this case?
A. Oh, I would imagine -- I wasn't arguing they filed one. I just didn't remember when. I -- they -- they studied humans, so I'm quite sure they would have filed an IND.
Q. Okay.. And do you know whether any humans have been studied before this IND was filed in the

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United States?
A. No, I don't know.
Oh, in the United States?
Q. Yes.
A. Oh, I certainly hope not.
Q. Okay. Do you know whether --
A. I hope they didn't study it before they had an IND.
Q. Okay. And do you know how many -- whether they had filed -- strike that.
Do you know whether they had studied sildenafil in any humans outside of the United States before filing their IND on September 7th, 1994?
A. I don't believe so, but I -- I'm not certain.
Q. So you weren't aware that they had started studies of sildenafil in humans in Europe prior to that date?
A. I do not know if it was before 1994, but I -- I don't think it would have been in the United States before 1994.
Q. Okay. Do you know -- well, strike that.
If you look at the second paragraph under "Interactions With the FDA," it says that "The Division of Cardio-Renal Drug Products."
That's DCRDP, right?

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A. Yes.
Q. Okay. So "DCRDP expressed the basic requirements of the long-term safety database for an NCE and PRN drug," right?
A. Yes.
Q. What is NCE?
A. New chemical entity.
Q. And PRN drug?
A. One that will be taken as needed.
Q. Okay. It says, "Based on the outcome of the muscle aches and color vision disturbances, DCRDP recommended that 1,000 to 2,000 patients should be exposed to the drug, of which 500 to 1,000 should have taken it for one year."
Do you see that?
A. Yes, you read it correctly.
Q. Okay. The reference to color vision disturbances, do you know what that refers to?
A. The blue reports in the IND patients.
Q. Okay. And that was known to Pfizer and FDA before the application was ever submitted to FDA, correct?
A. Now you're referring to the new drug application.
Q. Yeah, correct.

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A. Yes, because it says "1995."
Q. Okay.
A. Yes.
Q. And do you know what type of testing was done to investigate the color vision disturbances that had been seen before the drug was filed, the drug application was filed?
A. What kind of -- what kind --
Q. Testing was done to investigate?
A. Well, the initial reports were simply patient reports of this. And then I believe they had entry -- they changed the entry criteria to include one of the battery -- one of the color battery testings as a condition for the continued studies. But I believe the initial reports were patient reports, spontaneous patient reports.
Q. Okay. Let me -- let me repeat my question.
Do you know what testing Pfizer did before submitting the NDA to investigate the color vision disturbances?
A. No.
(Exhibit No. 5 was marked for identification.)
BY MS. LESKIN:
Q. I give you what we've marked as Exhibit 5, which is Appendix XII to the NDA, entitled "Sildenafil,

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Visual Summary."
Have you seen this document before?
A. No. I'm confused by the documents, though, because these have an approved date in '97 on them. So I'm confused.
Q. I'm sorry. You're referring to what?
A. They have approval date stamped of August '97 on them, so I'm still a little confused how these interact -- how these relate to the '98 FDA approval.
MR. ALTMAN: Objection; foundation, too. I -- what is this out of it? This says "Appendix XII." Is this part of the NDA here?
BY MS. LESKIN:
Q. I'll refer you back to Exhibit 4, Doctor. And if you look at the last page of Exhibit 4, which is the index.
A. Exhibit 4, last page.
Q. You'll see under the listing for appendices, Appendix XII says "Visual Summary"?
A. Appendix XII.
I see that. I'm just confused by the approval stamp date of a year before the NDA was approved.
Q. Okay.
MR. BECNEL: Let me enter an objection now. This document has the 28th of August 1997 where

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it says "approved." And the index that you've given us, Counsel, is for what year? What year is this index from?
MS. LESKIN: Is that your objection?
MR. BECNEL: No. I'm asking you to explain what --
JUDGE BORG: Well, is -- is there -- is there a date on the exhibit?
MR. BECNEL: No.
MS. LESKIN: It's the index to the NDA, Your Honor.
MR. BECNEL: Yeah. It doesn't make any difference. I want to know what year are you alleging that you've given this witness an index for that makes reference to something in the 28th of August 1997. That's all I'm asking.
BY MS. LESKIN:
Q. Doctor, do you know when the NDA --
MR. BECNEL: No, no, Counsel. I --
MS. LESKIN: Let me set my --
MR. BECNEL: Then I'll object to the --
MS. LESKIN: Let me set my foundation.
MR. BECNEL: I'll object to the use of the document.
JUDGE BORG: Okay.

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MS. LESKIN: Can I ask a foundation question?
JUDGE BORG: You can.
BY MS. LESKIN:
Q. Doctor, do you know when the NDA was filed in this case?
A. I know it was approved in March of '98, and it was -- yeah, it was filed at the end of '97 -- in six months -- I think it was the fall of '97. I'll find the date. I think I saw -- just saw it in here. But I think it was in the fall of '97. Let me see. That's my recollection.
Q. Okay. You want to find the date?
JUDGE BORG: Ms. Leskin, do you know the date?
MS. LESKIN: I believe it was sometime around --
JUDGE BORG: Okay.
MS. LESKIN: -- August, the end of August or September.
JUDGE BORG: No, no, I just wondered if you knew the date. I --
MS. LESKIN: Yes. And I'm happy to represent that it was late August, early September, 1997.
MR. BECNEL: Your Honor, my only thing is, is trying to connect whether one is out of order or not out of order.

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MS. LESKIN: It is not out of order. I will represent to you that Exhibit 4 is the index to the NDA as filed with the Food and Drug Administration; that Exhibit 3 is an excerpt from the NDA as filed with the Food and Drug Administration; and that Exhibit 5 is an excerpt from the NDA as filed with the Food and Drug Administration. I'm not trying to play games.
THE WITNESS: Well, okay.
MS. LESKIN: Trying to find out if the witness reviewed these documents.
THE WITNESS: Okay. Well, you -- actually the approval date was September -- I mean the submission date was September 29th, 1997.
MS. LESKIN: Okay.
THE VIDEOGRAPHER: Doctor, your mic.
THE WITNESS: Okay. I'll repeat it. Just one second.
The submission was, as I thought, in the -- in the fall of the previous year. And the specific date is September 29th, 1997.
BY MS. LESKIN:
Q. Okay. And prior to filing an application with the Food and Drug Administration, you know that companies go through an internal approval process for

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the documents that they file with the government, correct?
A. Yes. I've just never seen a different approval date stamped on a document that actually went to the FDA.
Q. Okay.
A. That I've never saw. I've never seen that before.
Q. Okay.
A. So I just --
Q. I will represent to you that these are excerpts of documents that were -- of the NDA that was filed with the Food and Drug Administration.
MS. LESKIN: I think we have answered all the objections. Okay.
MR. ALTMAN: I just need to make one other statement, that part of the problem is, too, Lori, is that if you look at Exhibits 3 and 4, they're stamped "Grant/Pfizer" and a Bates number.
MS. LESKIN: That is correct.
MR. ALTMAN: And Exhibit 5 does not have that legend, which --
MS. LESKIN: That's correct.
MR. ALTMAN: -- also makes it confusing as to whether this is all part of one continuous stream.

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That's part -- just part of the confusion here, that they have different Bates numbers and different legends.
MS. LESKIN: I'll represent to you that the way that these documents were produced in this litigation is that there were cases that were on -- that were filed prior to the MDL being created. The NDA was made available to plaintiffs' counsel in that litigation. They selected documents to be copied. Those documents were copied and Bates stamped. Those have there the legend "Grant/Pfizer docs."
Subsequent to that, additional document requests were made, additional review was made, and additional documents were requested to be copied. Those documents contain different Bates numbers.
So the fact that they -- I'm not representing that they were produced, though they were copied and therefore Bates stamped in order. These are all excerpts from the same Food and Drug Administration NDA.
JUDGE BORG: That's sufficiently confusing. Okay.
MS. LESKIN: It's because we Bates stamp numbers based on --

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JUDGE BORG: No, no. I understand.
MS. LESKIN: -- what they copied, not based on how they were made available.
MR. ALTMAN: I'm not -- I just -- I guess -- I think we just need to put on an objection just to the extent that I'm concerned that these productions were done at separate points in time, but the Bates numbers have been woven together. And whether this truly represents a complete continuous, I don't have any way of knowing that.
MS. LESKIN: We have made available -- from the beginning of this litigation, we have offered to make the NDA available. Plaintiffs have chose -- in this MDL, have chosen not to avail themselves of that. That's not our problem.
MR. BECNEL: It is your problem to make it understandable because of the production. That's your requirement.
MS.. LESKIN: You produced -- we made the documents available. You copied them. We Bates stamped them based on what copies counsel wanted. Zoe Littlepage is a member of your steering committee. She was responsible for identifying the documents as they were made available. She didn't copy the entire NDA. You can talk to

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Ms. Littlepage.
MR. ALTMAN: I guess there's one question that can probably --
Can we take it that even though the NDA as it was produced may not be complete because it wasn't all selected, that at least it is in the exact correct order it would have been in the NDA? I mean, you've basically pulled out pieces of the NDA that have -- let me ask it a different way.
We've got, I don't know, 20,000 -- at least 20,000 pages of an NDA here.. But we didn't get -- you're saying we didn't get the entire NDA. And I say that because the Bates number of Exhibit 5 is 19569. So one would assume --
Is it a true statement that while we may not have every page of the NDA up to that point, that whatever, the 20,000 pages up to this point, are in the exact order they were in the NDA?
MS. LESKIN: No, that's not a reasonable assumption because that's not how they were copied. That's not how they were requested. There were several times Ms. Littlepage came, selected documents, came back, selected more documents, in different litigations at different points in time. All of those documents were made -- then made

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available to the steering committee in the MDL when the MDL was created.
MR. ALTMAN: Okay. So if we go in Bates number order, we're not going to see whatever was selected necessarily in the order in the NDA.
MS. LESKIN: I can't make that representation without going back and seeing what the first 20,000 pages look like.
MR. ALTMAN: Okay.
MS. LESKIN: I can find out. We can talk about that offline.
MR. ALTMAN: That's fine.
MS. LESKIN: That was -- that was the --
MR. ALTMAN: I just wanted to understand the context.
MS. LESKIN: That was the request.
JUDGE BORG: Let's get going.
MR. OVERHOLTZ: All right. We'll just have an objection to this document, obviously, at trial. They'll have to lay a foundation.
JUDGE BORG: Yeah.
BY MS. LESKIN:
Q. Dr. Blume, let's go back to Exhibit 5. Have you seen this document before?
A. I believe so. I believe so.

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Q. And did you review this in developing your opinion?
A. I believe I looked through it. I mean, I did look over the -- what was known at the time of NDA approval, yes.
Q. Now, the provision of the federal statute that governs the filing and review and approval of an NDA is 21 USC 355, correct? Yes?
A. Yes.
Q. Okay. And you're not -- well, let me ask you this.
Are you offering an opinion in this case as to whether or not Pfizer complied with Section 355 in submitting its NDA?
A. The NDA was approved by the FDA.
Q. Okay.
A. So I would -- I am not going to argue that they filed the NDA appropriately..
Q. Inappropriately, you mean?
A. I'm not going to argue that it wasn't filed appropriately. FDA approved it.
Q. And you're not offering an opinion in this case that FDA was wrong when they approved this NDA, are you?
A. No.
Q. And you're not offering an opinion that FDA

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should withdraw this NDA, are you?
A. Well, I haven't offered that opinion, no.
Q. Okay. And you're not going to in this case, are you?
A. I have -- based on what the information I have so far, no.
Q. And you're aware that subsequent to the approval of the Viagra NDA that the FDA evaluated a separate NDA for sildenafil for use with -- in pulmonary arterial hypertension patients, correct?
A. Yes. I have that referenced in my report.
Q. Okay. And that's marketed today as Revatio --
A. Revatio.
Q. -- correct?
A. Yes, that is correct.
Q. And the FDA approved that NDA?
A. June of 2005.
Q. And you're not offering an opinion in this litigation that the FDA was wrong when they approved the NDA for Revatio, are you?
A. I am not.
Q. And you're not offering an opinion in this case that Pfizer violated any federal statute in submitting its application for Revatio, are you?
A. No. I've never said that at all in my report.

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Q. I just --
A. I don't know where you're getting this.. No.
Q. I want to make sure that I understand your report and your opinions.
MR. BECNEL: Counsel, I'm trying to figure out: Why you are asking questions that's not in her report, that's not the subject of this MDL in any way, shape, and form? Why are we doing this?
BY MS. LESKIN:
Q. Now, under Section 355 there's several grounds that Congress has prescribed for refusing the approval of an NDA, right?
A. Yes..
Q. And the FDA is required to deny the application if it does not include adequate tests to show that the drug is safe, correct?
A. Yes.
Q. And the FDA is required to deny an NDA if the testing that's submitted shows that the drug is unsafe, correct?
A. What did you say the first one was? Not safe and then unsafe?
Q. No. The first one I asked was whether -- well, let me rephrase, then.
The first question I asked you was: The FDA is

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required to deny the application if it does not include adequate tests to show that the drug is safe, right?
A. Right.
Q. Next part that I'm asking you is: The FDA is required to deny the application if the testing shows that the drug is unsafe?
A. Yes. Product has to be safe and effective to be approved.
Q. Okay. And if there's insufficient information to determine whether the drug is safe, the FDA is required to deny the application, correct?
A. Yes.
Q. At the time that the FDA approved the Viagra NDA, it also approved the label for Viagra, correct?
A. Of course. NDA approval must include the FDA-approved launch label, yes.
Q. Okay. Is it your opinion or are you offering an opinion in this case that the label at the time of approval was in any way inadequate?
A. I haven't offered that opinion at all.
Q. Okay. In your report, and I think even earlier today, we talked about the population of patients in a clinical trial database as compared to the real world. Right?
A. Yes.

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Q. And do you know how the population in the Viagra clinical trial database compares with the population in the real world?
A. Somewhat. I mean, the NDA is a -- is a relatively modest population. I think it only had about 4,000 patients in it, and some of those patients would have been on placebo therapy. So it is not a very big NDA. And my understanding from the correspondence between the company and the FDA and between some of the citizen's petitions is that several of the populations of concern were omitted from the clinical trials. Cardiovascular risk factors, some of the advanced diabetic populations were omitted from the Phase III patients.
Q. When you say that CV risk factors were omitted, what do you mean by that?
A. That patients who had marked hepatic dysfunction, marked renal dysfunction, and a listing of cardiovascular coincidental events were omitted from the -- from the control clinical trials.
Q. What's the basis for that statement?
A. The -- well, I think we have the inclusion criteria in one of the documents for the Phase III trials, and FDA denied one of the citizen's petitions that requested those omitted patient criteria be

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included in the -- be included in the warnings and black box, and FDA denied that even though those populations had not been fully studied in the NDA students.
Q. Do you know whether that information is currently included in the label for Viagra?
A. I have it. I'll look right now. What -- if what information? The exclusion criteria?
Q. Yes. You said that the FDA denied a public citizen's petition, so I'm asking --
A. Yes, it is -- it is in the label. They asked that it be put in a more prominent part of the label. And I believe that FDA denied it because they said it was already in another section of the label. So, yes, it -- it was included. They were asking for a more prominent spot. But I'm answering your question regarding exclusion -- exclusionary criteria in the critical trials.
Q. Okay. I'm going to give you what we're marking as Exhibit 6, which is the August 2008 version of the label for Viagra.
MS. LESKIN: Do you want a copy?
(Exhibit No. 6 was marked for identification.)
BY MS. LESKIN:
Q. I take it you've seen this before. Correct?
A. I have this cited in my report.

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Q. Okay. So you've seen this before, correct?
A. Yes.
Q. Okay. And I'd like to direct your attention, if I may, to page 12. And you'll note this is under the warning section, correct?
A. Yes.
Q. Now, there's four bullets there at the top of page 12. Are those the exclusion criteria you're referring to?
A. Those are the cardiovascular ones.
Q. Okay. And that's patients with a myocardial infarction?
A. I'm sorry. And also the retinis -- retinitis pigmentosa.
Q. Okay. And the cardiovascular ones that you referred to are myocardial infarction, stroke, or life-threatening arrhythmia within the last six months, right?
A. Uh-huh, yes.
Q. And resting hypotension or hypertension?
A. Yes.
Q. Meaning below 90 over 50 or over 170 over 110?
A. Yes.
Q. And patients with cardiac failure or coronary artery disease causing unstable angina, correct?

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A. Yes.
Q. Okay. Are there any other exclusion criteria regarding to cardiovascular factors that you're referring to?
A. Well, there were certain concomitant medications that were excluded.
Q. Like nitrates?
A. Of course.
Q. And that's a contraindication, correct?
A. Of course.
Q. And that's been a contraindication in the label since it was -- approval, correct?
A. Oh, yeah. That's -- I hope so. Yeah.
MS. LESKIN: I'm going to mark here as Exhibit 7 a copy of the joint clinical review put out by the Food and Drug Administration dated -- the review date is January 22nd, 1998.
(Exhibit No. 7 was marked for identification.)
BY MS. LESKIN:
Q. Have you seen this document before?
A. We -- we have a medical review. I -- I don't recall if I had the joint medical review, though.
Q. And when it approves a application, the FDA creates a review of all the information, correct? They're required to create a written document justifying

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the approval?
A. Summary basis of approval, yes.
Q. Okay. And are you aware that this document, the joint clinical review, was published on the FDA website following the approval of Viagra?
A. I don't remember the joint review. I remember a medical review, but I don't remember a joint clinical review.. I -- I just don't recall it.
Q. Okay. Are these in the documents that plaintiffs provided to you?
A. I believe I have the medical review that I obtained from the website. And I also believe they provided me NDA documents relating to a medical review.. I just don't recall one that was titled "Joint Review.."
Q. Okay.
MR. ALTMAN: I'm going to -- I think we need to object to foundation. Are you saying you got these off the FDA website?
MS. LESKIN: This is the FDA joint clinical review. It's available on the website. But this is the FDA joint clinical review.
MR. ALTMAN: Okay. Can you tell me where on the FDA website?
MS. LESKIN: FDA.gov, search for Viagra, look for history of approval, you'll find it. It's still

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up there.
BY MS. LESKIN:
Q. If you look at page 13.
MR. ALTMAN: I don't see it.
THE WITNESS: I'm sorry?
BY MS. LESKIN:
Q. If you look at page 13.
A. Okay.
Q. Okay. You look at the top, and it says it's referring to Table 8?
A. Yes.
Q. And that's a summary of the numbers of subjects exposed in the sponsor's development program, correct?
A. Yes.
Q. And you said that there was about 4,000 patients, but some of those had taken placebo?
A. Yeah. That was my recollection.
Q. Okay. What's the number actually?
A. 4,526.
Q. And those patients had all taken sildenafil, correct?
A. Taken sildenafil. Let's see. The column -- 3,003 and 3 -- and 769 is 3,772.
Okay. 3,772.
Q. Plus 178 from the Japanese studies?

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A. Plus the foreign data. Yeah. It was a relatively modest NDA.
Q. It's about the size of an NDA for an antihypertensive product, correct?
A. Well, they're bigger now. I mean, 4,000 active patients is a relatively small NDA.
Q. Okay. As of 1998, was that about the size of a hypertension study?
A. Yeah. Generally they were between five and seven thousand during that time frame.
Q. If you look at page 15.
A. I mean, for a -- for a new chemical entity, it is not a big NDA.
Q. Okay. If you look at page 15.
In section 5.3, the FDA notes that this is comparable to the size of a typical database for a new antihypertensive agent.
Do you see that reference?
A. Yeah. It's just --
Q. Take a look at page 14 on that -- in that document for me. Do you see Table 11?
A. To go back to your earlier question, I think FDA is referring in this to the adequacy of the patients on subject years. I think that you need -- this is a narrow interpretation of what they're saying. And

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they're looking at how many patients were in it for various points of time. And I think that the FDA comment also says, while this level of safety assessment is adequate, it's a matter of judgment. So I don't think they're referring in this paragraph to the number 4,000.
Q. Okay.
A. They're referring to how many of those patients were used in longer study designs.
Q. Okay. But you're not offering an opinion that the size of the database was inadequate for approval, are you?
A. I'm not arguing -- okay. I -- again, I'm not arguing that this product was approved. I'm just saying, 4,000 patients on a new chemical entity for a new indication is a rather modest NDA. But the NDA was approved.
Q. Okay. And you're not offering an opinion that the size of the database was inadequate for approval, are you?
A. I am -- I agree with you that the NDA was approved and FDA found the database adequate for approval.
JUDGE BORG: You've got about four minutes.
MS. LESKIN: Okay.

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BY MS. LESKIN:
Q. Turn to page 14, please.
MS. LESKIN: Thank you.
BY MS. LESKIN:
Q. See Table 11 up there on top?
A. I see, yes.
Q. And according to -- that next table representing the disease status of patients within the study, correct?
A. In the placebo-controlled and open-label studies, yes.
Q. Okay. And according to this table, 25 percent in the placebo-controlled and 27 percent of the patients in the open-label studies had hypertension, correct?
A. I can't read the black.
Q. It -- I'll represent it says "PC" and "OL," and then it has the "N."
A. And that's percentage?
Q. That's percentage --
A. Percentage of the --
Q. -- if you look at the top.
A. Yes, 25 had hypertension in one, and 27 in the other.
Q. Okay. Do you know what the percentage of men with hypertension is in the general population?

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A. I know it's 40 percent in 50-year-olds. And I believe it goes higher with each decade, although that is complicated by those that are on antihypertensives.
Q. You see that diabetes in the clinical study was 18 and 19 percent?
A. Yes.
Q. Do you know what the underlying medical percentage in the population is for men?
A. No.
Q. And you see it says 14 and 15 percent of the men in the studies had hyperlipidemia? Do you see that?
A. Well, go back and comment on your question, the hypertension.
They specifically excluded types of -- I mean the more severe forms of hypertension. So that probably explains why these are only at 25 and 27 percent, because they took out the really -- the high-level hypertensives before the studies. And that agree -- that also goes for the rest of these cardiovascular-related. So these end-point percentages may well be under the average across all populations.
Q. Well, do you know what the background rate for diabetes is among men?
A. No.
Q. Are you aware that the -- Massachusetts Male

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Aging Study found 7 percent of that population had diabetes?
MR. BECNEL: I'm going to enter an objection. She just told you she didn't know. And then you asked the question: Do you know of what this study says?
JUDGE BORG: That -- that's not repetitious, and it's overruled.
Do you understand, and are you able to answer the question?
THE WITNESS: I know that it -- okay. I didn't -- I didn't know they said 7 percent.
I have used the term 6 percent across the United States population.
BY MS. LESKIN:
Q. And the Massachusetts Male Aging Study specifically looked at the pop -- the incident rate in older men, correct?
A. I don't know. I don't know.
Q. Are you familiar with the study?
A. Not particularly. I just use the number 6 percent.
Q. Okay. And across the entire population?
A. Yes.
Q. Okay. Going back to hyperlipidemia.

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JUDGE BORG: Two minutes. Is this a good time?
MS. LESKIN: Let me finish these last two --
JUDGE BORG: Okay.
MS. LESKIN: -- and I'll be done.
JUDGE BORG: All right.
BY MS. LESKIN:
Q. Hyperlipidemia, that's high cholesterol, correct?
A. Or high triglycerides.
Q. Okay. And 14 or 15 percent of the men in the clinical database had hyperlipidemia, correct?
A. Yes.
Q. And cardiovascular disease, 14, 15 percent of the men in the clinical database had cardiovascular disease, correct?
A. Correct.
Q. Do you know what the population of the men -- of the background rate in older men is of either hyperlipidemia or cardiovascular disease?
A. No. But I have a question.
The open-label study, did this conclude their volunteers, the healthy volunteer studies? Because if the healthy volunteers are included in this number, then all the ages are diluted because they will be younger than the intended population for this drug. So we can't

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merge them.
MS. LESKIN: Okay. We'll come back to that as soon as we change the tape.
THE VIDEOGRAPHER: We're off the video record.
(There was a discussion off the record.
Luncheon recess from 12:14 p.m. to 12:46 p.m.)
THE VIDEOGRAPHER: We are back on the video record.
MR. ALTMAN: Lori, before you get started, just two brief issues.
I just want to note for the record that we were able to locate that FDA document, and that it is not in the regular place where those documents would be kept on the FDA website. It was just in some other place. I just want to clear up that it is not in the regular place.
The second issue is: You asked for a copy of the data and charts provided to Dr. Blume. I'm presenting you with a CD that has all of those materials on it.
MS. LESKIN: Thank you.
JUDGE BORG: Is that all? Bless you.
MR. ALTMAN: Do you want more?
JUDGE BORG: No. But I think I want you to do all the talking..

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MS. LESKIN: For them, you mean?
JUDGE BORG: That's why I said it.
Well, no, I'd let him do it for everybody.
All right. Ms. Leskin, you may proceed. We're back on.
MS. LESKIN: Just to clarify, though, the FDA document we're talking about is a joint clinical review, right?
MR. ALTMAN: Yes. It's just that there was a regular place where one would expect to find those documents, and we've agreed you had to show me where to find the documents --
MS. LESKIN: Right. On the website, though?
MR. ALTMAN: On the website. But it is not where such documents are normally kept.
MS. LESKIN: Okay.
THE WITNESS: And I also need to clarify, I did not make another copy of my hard drive for you. If it's requested, I can make another copy of the hard drive. The disk that I gave you obviously does not include the hard-drive documents.
MS. LESKIN: Okay.
THE WITNESS: The hard-drive documents, I can make another -- I can make a hard drive for you if -- if you request it. But it is the Pfizer

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production documents.
BY MS. LESKIN:
Q. Okay. And do you have any kind of index as to what documents are on that drive?
A. Yes, I think so.
Q. Okay.
A. I think so.
Q. If we can get a copy, at least, of the index of the documents on the drive, that would -- instead of getting a whole new hard drive from you.
MR. OVERHOLTZ: That's fine.
MR. ALTMAN: It's going to be the production through -- it's -- the only thing that's not going to be in it is, like, the last Pfizer production.
MS. LESKIN: Okay. That's fine.
THE WITNESS: So you still want it?
MS. LESKIN: Yeah, I'd still like the index.
MR. OVERHOLTZ: We'll get it done.
MS. LESKIN: At a break.
THE WITNESS: We'll get it at a break. I will.
MS. LESKIN: Yeah.
BY MS. LESKIN:
Q. Dr. Blume, when in your -- is it your opinion that a signal -- well, strike that.
Is it your opinion that there has been a

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signal, a safety signal, for NAION and sildenafil?
A. Yes.
Q. And in your opinion, when did that signal occur?
A. I think a signal for visual disturbances, including vision loss, was apparent by 2002.
Q. Now, when you say "vision loss," does that include things other than NAION?
A. Well, I -- it includes permanent vision loss, I think. Yeah.
Q. Does that include permanent vision loss due to things other than NAION?
A. It includes also the terms reported as ION.
Q. So NAION, ION. Anything else?
A. I think that's it.
Q. Okay. So it's your opinion that as of 2002 there was a safety signal for NAION and ION. Is that fair to say?
A. Right, yes.
Q. When you say by -- when it was apparent by 2002, is there a particular time in 2002 that it became apparent?
A. No. I don't think I looked at it by month.
Q. Okay.
A. No. Well, let me clarify that in reality in

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2000 there was an AERS database signal for the ION term. So by 2000 there was a post-marketing -- based on that alone, there was a -- there was a signal.
Q. Okay. When you say by 2000 there was an AERS database signal, for NAION and ION?
A. Well, it's the ION term.
Q. The ION term?
A. Right.
Q. What was that -- what's that based on?
A. When I asked Mr. Altman to evaluate the AERS databases we discussed earlier this morning, beginning in 2001 Viagra -- the signal that I -- I would have detected is that Viagra had the most number of events beginning in 2000, and it maintained that total number of cumulative events throughout the period to 2005.
Q. Now, when you say it has the most number of events, what do you mean by that?
A. Had the greatest -- of all the products in the AERS database, Viagra had the greatest number of ION events, beginning in 2000, cumulative number events beginning in 2000. And that continued through my period of interest, through 2005.
Q. How many ION events did Viagra have in 2000?
MR. ALTMAN: Objection; vague.
THE WITNESS: I did not -- I started the

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database evaluation in '98 because it was approved in '98. And AERS has two terms in '98, total of five terms in '99, and 12 terms in 2000.

MR. ALTMAN: I had an objection. I don't think it was heard. But I had objected as vague. And my only point is: Are you talking about -- when you said how many NAION events, are you talking about just in the AERS database?

MS.. LESKIN: The witness was able to understand the question.

JUDGE BORG: Yeah. She answered it.

MR. ALTMAN: Well, I don't think she heard me object to know whether -- I just want to make sure that she was answering in term of context of AERS. That's all. I'm sorry.

JUDGE BORG: Okay.

THE WITNESS: Well, I'm intending that to be the context of AERS, yes. And in 2000, those 12 represented about 15 percent of the total ION events in the overall AERS database.

BY MS. LESKIN:

Q. Now, when you say there is two terms in '98 and five terms in '99, what's a term?

A. Reports.

Q. Okay. So according to the data that you have,

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there were two NAION reports in nineteen ninety -- or ION reports in '98, and five reports in 1999, correct?

A. Correct.

Q. Have you looked at those reports?

A. No. I mean other than -- no. I did an evaluation of the total number of reports only.

Q. Well, let me ask you this.

Do you know if anyone at Pfizer -- excuse me -- looked at those reports?

A. I don't -- I think I recall seeing that Pfizer -- Pfizer correspondence about AERS. I don't recall if I remember it in '98 and '99.

But a signal, when one product is a contributor and is the largest contributor to a database, that alone is a signal.

Q. Okay.

A. And that position did not change for the next five years.

Q. Okay.

A. So in my interpretation, that is a signal.

Q. Okay. What do you base that on?

A. Well, again, FDA's definition, and the one that we are taught to use in industry, is anything that makes you look differently and anything that makes -- distinguishes your product from others, be it

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mechanistically or be it in a chemical category.

And Viagra comes into the market in mid '98, I believe, and within 18 months it has the largest number of ION-related events in the database. And in fact it is 15 percent of that database and is up to around 20 percent of it in 2001.

So ION events in the U.S. database are not distributed equally across all products, obviously, and the distribution is skewed to a couple products. And the largest of those products is Viagra.

Q. What percentage of the AERS database were Viagra adverse events of any type in 1998 -- well, strike that.

In 2000, what percentage of events in the AERS database were related to Viagra?

A. What -- I'm sorry. What percentage of AERS related to Viagra?

Q. Yes.

A. As what?

Q. In 2000, what related --

A. I don't understand what you're asking. But is it as a primary drug? A secondary drug? Is it a report that has it as a primary? A suspect? A serious suspect? I mean, how are -- how are you breaking that down?

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Q. Okay. Well, let's talk about the ION reports in 2000. You said there were 12 events reported, correct?

A. Yes.

Q.. What is Viagra for those events?

A. Suspect agent.

Q. Okay. So what percentage of adverse events in the AERS database in 2000 listed Viagra as a suspect agent?

A. Oh, I have no idea. I'm only -- I'm -- I'm focusing on a -- the ION events. It's of no relevance to me what percentage of all the Viagra events are in the database. What relevance is that to me? My interest is: Is there a signal for a very particular event? It doesn't matter to me if Viagra is causing cardiovascular events, different cardiovascular or different hepatic events. I'm focusing on ophthalmic events. If I focused on everything, I would never be able to drill into the data.

Q. What percentage of Viagra adverse events in 2000 were ION events?

A. Again, I have no idea, nor does that influence my opinion. My opinion is, when I look at an event -- when you work in a company and realize that you are receiving some events, and you want to know the -- put

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some context, as you say, into this event, one way of doing it is looking at your contribution to these events and all other drugs' contribution to this event. And what I would see is, there was a very definite difference with Viagra and the rest of the drugs. And that difference continued. So it wasn't one year that there was a difference, and then it disappeared. It was maintained.

MS. LESKIN: Move to strike as nonresponsive.

BY MS. LESKIN:

Q. My question --

MS. LESKIN: I'm sorry.

JUDGE BORG: Sustained. Go ahead.

BY MR. OVERHOLTZ:

Q. What percentage of Viagra adverse events in 2000 were ION events?

A. I thought I answered it. I don't know. And it isn't relevant to my opinion.

Q. What authority are you relying on to establish that the 12 events in 2000 identified a signal?

A. Okay. Again, a signal is anything that makes you look differently, an event.

Q. What authority are you relying on for that?

A. That's the FDA's definition of a signal.

Q. Where does it say that?

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A. Oh, I don't -- I don't know if it's in this current one or not. You know, I have been doing this for 30 years. And for 30 years I have done signal detection, looking at different databases to see if I see anything different or any change in something I've seen before.. And I believe that the definition they use here is, if you're seeing anything in excess of what you expected to see. In fact, I think you read that to me.

Well, if I look at this database using the government's AERS database, and I see that of the 80 events, 12 of them are Viagra, that is more events than I expected to see with one single drug. If I look at the database in 2001, and I see there's only 100 events in the database, and 21 of them are Viagra, again that is more than I anticipated to see based on all of the data I'm looking at. So even with this 2005 definition, I think we've defined a safety signal with the AERS database.

Q. Well, let's go back to that 2005 definition. That definition says, "Safety signal refers to a concern about an excess of adverse events compared to what would be expected to be associated with a product's use."

A. Exactly. The product was launched in mid '98, and there were two events. You didn't see any, as you've told me three times, in the -- as was told three

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times in the overview, on the clinical trial database. None were seen. So now it's on the market for a couple months, and there's two events. The following year, it's up to six events, and then up to 12 events. And that's the leading contributor. That's more than what I would have anticipated to see with a Viagra use.

MS. LESKIN: Move to strike. There was no question pending.

JUDGE BORG: Sustained.

MR. OVERHOLTZ: There was a question pending.

JUDGE BORG: No, no. There -- there --

MR. BECNEL: Yeah.

JUDGE BORG: The question was -- was asked, and the question was answered, and then it continued.

MR. OVERHOLTZ: She said, "Let's go back to that 2005 definition. It says, 'Safety signal refers to a concern about excess of adverse events compared to what would be expected to be associated with a product's use.'"

MS. LESKIN: Where's the question?

MR. OVERHOLTZ: And then looked at her.

MS. LESKIN: I actually didn't look at her.

MR. OVERHOLTZ: Were you making a statement?

MS. LESKIN: Well, she started speaking before --

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MR. OVERHOLTZ: You were just testifying on the record.

MS. LESKIN: Well, no, but I -- I read a statement. I did not yet ask a question. And the doctor started speaking.

Move to strike; no question pending. And I believe that was sustained.

MR. BECNEL: Objection.

MS. LESKIN: To?

MR. OVERHOLTZ: First of all, I don't -- I've never -- first of all, there's no authority in the rules to a move to strike during the deposition of a testimony. There is no authority for it. If you want to --

JUDGE BORG: For -- for what? The motion to strike?

MR. OVERHOLTZ: Motion to strike. If she wants to file objection, nonresponsive, that's one thing. A motion to strike is not an appropriate legal objection during a deposition. There is no legal authority of it in any case you will ever find reported during a deposition.

JUDGE BORG: The objection is limited to nonresponsive.

MR. OVERHOLTZ: That's correct.

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JUDGE BORG: By the way, that makes all other objections limited to privilege, nonresponsive, and form of the question. And I hear lots of objections that don't fit any of those three.
MR. OVERHOLTZ: You're right.
JUDGE BORG: Okay. Ms. Leskin, you can proceed.
MS. LESKIN: Thank you.
BY MS. LESKIN:
Q. Do you know how many men took Viagra in the first year it was on the market?
A. No.
Q. Do you know how many men in a population -- well, strike that.
Do you know how many men have taken Viagra since it has been on the market?
A. Oh, I recall seeing that in one of your records. I think it's 30 million. I think it's around there..
Q. So using that number of 30 million, do you know how many cases of NAION you would expect to see in a population of 30 million men over a 10-year period, just as background rate?
A. Well, I only have the two background studies. So if it's 10 in 100,000 or 2 in 100,000, 2 in

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100,000 -- 2 in 100,000 would be 20 in a million. 20 in a -- 60.
Q. And if you use the higher number?
A. Higher number was five times more than that, so that would be 300 million.
Q. 300?
A. 300. Sorry. And if these -- oh, sorry. I'll continue when you ask a question.
Q. Now, we talked about signals, and we said that once you have a signal, there's an obligation to investigate, correct?
A. I was just going to complete my answer to the last one. Can I do that?
Q. I think you answered the question.
The question was, what would be -- what you would expect. And you said 60 or 300. That was the only question that was asked, Doctor.
So my question now is: Once you have a signal, there's an obligation to investigate, correct?
A. Well, there's multiple obligations. One of the obligations is to investigate.
Q. Okay. Are you -- are you aware of what investigation Pfizer conducted in 2000?
A. No. I'm not aware of any.
Q. Is it your testimony that Pfizer did not

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conduct an investigation in 2000 or you're not aware of any?
A. I'm not aware of any investigation in 2000 or any studies done in 2000.
Q. Well, was the only study that -- the only way to investigate to do a study?
A. No. There's other ways.
Q. Is it your opinion that Pfizer should have done a study in 2000?
A. I think, yes, my -- my opinion is that certainly by 2001 or '2, when this pattern was confirmed, a study should have been conducted.
Q. What type of study should have been conducted?
A. Well, a study that would allow them to quantify -- I think Pfizer should have done two things beginning in 2000.
One is, of course, that the information should have been shared with prescribers and patients. Absolutely that should have been done. And then if they wanted to define further the risk of NAION, they could have begun a study that would have allowed them to compare NAION events in Viagra-treated patients with some sort of a control -- hopefully age and disease and other demographic-controlled control groups. But that study is certainly not necessary before they share the

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information with their prescribers and patients.
And by the time 2000 or two thousand -- the additional events in 2001 and 2002 were known, NAION should have been in the labeling or ION in the labeling.
MS. LESKIN: Objection; nonresponsive.
BY MS. LESKIN:
Q. My question was: What type of study should have been conducted?
MR.. OVERHOLTZ: She answered your question.
THE WITNESS: I thought I answered that.
MS. LESKIN: Okay. Well, I'll move to strike anything -- part of that answer that was not. And I'm going to ask my question and ask you to restrict your answer to my question.
BY MS. LESKIN:
Q. What type of study should have been conducted in 2000?
A. Well, in 2000 they should have reviewed the various options for this type of an event. They could -- they should have reviewed the ability in 2000 to do either a case-controlled study or a cohort-controlled study. And then making a decision of what was available to them in 2000, based on available databases, that study should have been initiated.
Q. Have you ever designed a case-control study?

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A. Oh, yeah. Yes.
Q. Okay. How long would a case -- well, let me ask you this..
How many patients would be required in a case-control study to determine whether there was an increased risk of NAION in patients taking Viagra?
A. Oh, it's depending on how you calculate it. I mean, it could be anywhere from -- could look for 300 patients all the way up to 150,000 patients.
Q. How long would a study like that take?
A. All depends on how much effort they put into the study, how many ophthalmologic sites they were willing to open.
Q. What's a range?
A. A couple years. A couple years. Maybe longer. We don't know because they didn't do it. But I would imagine a couple years.
Q. You're aware that currently Pfizer has started doing a case-crossover study --
A. Oh, yes.
Q. -- to investigate NAION, correct?
A. Yes, I'm aware they did start that last year.
Q. Okay. Do you know how long that study is estimated to take?
A. No.

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Q. And have you ever designed a cohort study?
A. We helped with the cohort study, designing it, with a client.. But there was also -- their people were also involved in it.
Q. How many --
A. And I think in this case it would -- a case-control study would probably be the study one would have to do. A cohort study would take forever. But a case-controlled study, I mean certainly people were doing those types of study in 2000. It should have been started then.
Q. What authority are you relying on for your opinion that the Pfizer should have started a case-control study in 2000?
A. That when safety signals are higher than what one anticipates, one needs to investigate it -- investigate. And that investigation can take a variety of venues, and one of those venues is, is to do a study.
Q. And what authority are you relying on that 12 reports is sufficient justification to start doing a case-control study?
A. Well, there was more than those 12 reports. We've been focused on the AERS database. But 12 reports is a safety signal, and it's a safety signal for an event that can lead to blindness. So it's a serious

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event, as it is -- as it is not a transient clinical -- clinically minor adverse event.
So when a signal was obtained in a population for which the use of the drug is recreational, and certainly not intended to either extend life or cure a disease, and the adverse event is -- can be permanent blindness, then certainly the benefit/risk would tilt toward doing a study to learn more about this event, not only to quantify the event, but also to do a study that would attempt to identify any particularly vulnerable subgroups. And that's why post-marketing studies are done.
Q. Now, you said to me that there's more than 12 events. We were only looking at AERS. Well, how many other events were there?
A. Well, if FDA tells you that AERS has only 1 percent to 10 percent of total events, so either -- at that point there was either 120 or 1,200 ION events.
Q. How many events were there as of 2000, Doctor?
MR. BECNEL: Objection; vague.
THE WITNESS: I thought I answered. There were 12 points to AERS, and FDA has -- has always cautioned, that's only 1 to 10 percent that have actually occurred.
BY MS. LESKIN:

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Q. That's estimated 1 to 10 percent, correct?
A. Well, that's the FDA's numbers.
Q. So you don't know, sitting here today, how many reports -- how many events there actually were in 2000, correct?
A. I can only quote to you what FDA uses in -- as their number, and it's 1 to 10 percent.
Q. Okay. So sitting here today, you don't know how many events there were in 2000?
MR. OVERHOLTZ: Object to the form; asked and answered, misstates the witness's testimony. She answered the question.
JUDGE BORG: She -- she -- it's overruled. She's not misstating anything. She's asking a question.
MR. OVERHOLTZ: Well, she asked the same question --
JUDGE BORG: It's not the same question. She --
MR. OVERHOLTZ: It's the exact same words.
JUDGE BORG: It is overruled. The question is asked. This witness --
Dr. Blume, are you able to answer it?
THE WITNESS: I -- I don't know where the number fell between 120 and 1,200.

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BY MS. LESKIN:
Q. Do you know it's at least 120?
A. Just based on what FDA says. You're -- I don't know what I don't know. No one knows. But because we try to be conservative in our safety handling with our drugs and with our potential patients, we use the estimate that FDA gives us: 1 to 10 percent are reported.
Q. But you don't know what the actual number is, right?
A. Okay.. I thought I've answered this. No, I don't know the actual number. But with 12 alone, I would have recommended it going into labeling.
Q. Did you look at the adverse events that were reported in 2000?
A. No. I know that they are serious suspect events.
Q. Did you look at the --
A. No.
Q. -- MedWatch forms?
A. I did not look at the MedWatch forms.
Q. Do you know if any of those 12 are duplicative?
A. The way in which we do these analyses, duplicates are ruled out.
Q. How do you know?

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A. Because Mr. Altman has done this repeatedly for me for years, and it's been the basis of NDA submissions. FDA has asked this same question. And the NDAs have been approved upon -- and using the materials he has given me with his evaluation of the AERS database has -- has been specifically questioned if there can be duplicates.
Q. Is it possible that the company was unaware if there were duplicate reports?
A. I have no idea what the company knew in 2000 about their 12 events. I have no idea.
Q. And that's because you never looked at the MedWatch reports that were submitted to FDA, correct?
A. No, because I'm looking for signal detection. And you can demean and denigrate, dilute AERS data all you want, but the basis is, it serves as the basis for product withdrawals and product labelings. And based on this, they had a signal in 2000 using the same criteria that we use for making decisions on drug -- for drug product labeling.
Q. What case -- what product has been withdrawn from the market based on 12 adverse event reports where no one looked at the MedWatch reports?
A. I didn't say they were withdrawn based on 12. I said the AERS database is the basis for making

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decisions relating to drug labeling changes and drug withdrawals.
Q. And that -- that's -- the AERS database serves as a starting point, correct?
A. Oh, I don't know if it's just a starting point. I don't know where you're -- what authority you're basing that we make decisions using only the AERS as a -- as a starting point.
Q. Are you telling me that people have made decisions on the AERS database without ever looking at the underlying reports?
A. No, I didn't say that either. But I'm looking at signal detection now for labeling purposes. And the product had more than anyone else in the database, and they were coded as serious and suspect agents.
In addition to that, by 2000 and later there had been independent literature reports, and there had been other reports. So we're not talking just about the AERS data.
Q. Okay. Tell me what literature reports there were in 2000.
A. Okay. I think the original -- well, I'll -- I'll just do this in order.
Okay. I begin the literature review on page 16, dealing with ophthalmologic events. And I

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believe the first event that everyone talks about is the Egan and Pomeranz.
Q. Where is that on page 16, Doctor?
A. Oh, I don't know if it's there. I was just -- mentioned that -- I think it comes a little bit later. But Egan and Pomeranz was in 2000.
Q. I'll direct your attention to page 13 of your report.
A. I'm sorry?
Q. Top of page 13, is that where you refer to Egan and Pomeranz?
A. Yes.
Q. Okay.
A. Okay.
Q. Is that the first case --
A. Well, I refer to them -- I refer to them separate -- several times.
Q. Okay.
A. I think. I think that was the first case that was reported.
Q. Okay. Is that report in the AERS database?
A. I think so. I think so.
Q. So that's one of the 12 that you --
A. I believe so. I believe --
Q. Okay.

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A. I believe I recall that, reading that.
Q. Okay. So what other literature reports were in there in 2000?
A. Well, I think I gave between 2000, 2001, and 2002 when I gave my review.
Q. Okay. What other literature?
A. Okay. Cunningham and Smith is 2001.
Q. Is that in the FDA AERS database?
A. I don't -- I don't -- no. It's in the Egan and Pomeranz. Boshier in 2002. Dheer in 2002.
Q. Are those reports in the FDA database?
A. I don't think so, no.
Q. Did you look?
A. I did not look at the underlying events, underlying MedWatch forms, in the FDA's database.
Q. So when you say you don't think that they're in the FD AERS database, what's the basis for that opinion?
A. I recall reading it in the Pfizer documents, that Dheer and Boshier had not been included.
THE REPORTER: Dheer and?
THE WITNESS: Boshier, B-o -- B-o-s-h-i-e-r.
BY MS. LESKIN:
Q. Find me that document, please.
A. Pfizer documents? Oh, I don't have it cited here.

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Q. You just made a statement, Doctor, that these reports are not in the AERS database. I want to see the document you're relying on --
A. And I will -- and I will attempt to find it --
(Reporter clarification.)
BY MS. LESKIN:
Q. Doctor, you just testified that the Dheer and Boshier case reports were not included in the AERS database. What is the basis for that opinion?
A. Because I thought I recalled in the Pfizer documents that they had noted that the original -- those two reports, the Indian report and the Boshier report, had not been included in the early AERS data.
Q. Okay. When you define early AERS data, when is that?
A. Well, I think they were talking about prior to 2005.
Q. Okay.
A. But I don't recall the specific year. But my point is --
Q. No, no. My question is: What document says that?
A. I'll have to look. I don't --
Q. I'd like you to find -- at the break --
A. I'm sure you would. And I will attempt to look

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at it.
But my point was, in bringing this up is, you asked me --
Q. Doctor, there's no question pending.
A.. Well, you asked me what a signal was. I'm answering your question.
JUDGE BORG: No, no. I'm sorry. I didn't get that question. Is that back in there, where she asked for a signal?
MS. LESKIN: I -- I haven't asked that question in at least 20 minutes.
JUDGE BORG: Well, I'm asking the court reporter. The last question that I heard was, "Can you find the document?" You've indicated you will attempt to do that.
THE WITNESS: I will. I will.
JUDGE BORG: Okay. That's the last question I've got.
THE WITNESS: But I was responding. She interrupted me when I was responding to an earlier question.
JUDGE BORG: Okay. Well, there isn't a question to you. Yeah. Well, that wasn't -- yeah. We do them one at a time here. And -- and you're --
By the way, the attorneys on the other side are

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going to get to ask you questions today.
THE WITNESS: I understand.
JUDGE BORG: Okay.
BY MS. LESKIN:
Q. When did you receive this chart from Mr. Altman?
A. Oh, gee. I don't know. I don't know. I'll have to check. I don't know when I got it.
Q. Was it before or after you signed your report in this case?
A. I think it was after.
Q. So that information that you have in your hand did not form the basis for the opinions as expressed in your expert report dated December 1st, 2008; is that fair to say?
A. No, probably not. It corroborates it, but no. I had the opinion long before I saw any of the -- yeah, I had the opinion earlier.
Q. Okay. So putting aside the report that Mr. Altman provided to you, what other basis do you have for your testimony that a signal existed in 2000?
A. Well, I've always said 2000 to 2002. Okay?
Q. Well, which is it?
A. It's that time frame, because of the -- what I'm going to talk to you about. Okay?

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I looked over a variety of issues. One of the things that I looked at were the safety update reports who included blindness, either temporary blindness or permanent blindness. Beginning with safety update No. 2 and continuing with all safety updates after that, there were reports of blindness. Also beginning with safety update 2, which is a 1998, and 1999 in safety update 3, there were reports of rechallenge information. So that alone is another signal. You had the reports, reported them in the safety update. And included with that information were reports of rechallenges. One rechallenge alone can be evidence for the need to change a label.

Q. Okay. Show me the report of rechallenge.

A. Well, it's a safety -- well, okay. I think I have a -- it's a couple different places.

If you look at page 28, I talk about a man in 2000 who had positive rechallenge on three separate occasions using Viagra, in blindness. Then --

Q. I'm sorry. You said a positive rechallenge on three separate occasions.. What is the date of that report?

A. October 10th, 2000.

Q. And what's the event that's being reported there?

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A. Blindness.

Q. Is that NAION?

A. I don't recall. But I recall saying to you that I looked at temporary or permanent blindness. And since you don't have permanent blindness in your labeling either, that should have gone in there as well.

And then I do a review of the periodic safety updates, and there were rechallenge events relating to blindness in, as I said, safety update 2 and safety update 4.

Q. Before we get there, I just want to ask you a question, Doctor.

Is it your testimony -- see, I'm -- I'm having a problem here, given some of the objections that plaintiffs made.

Is your report focusing on blindness or is your report focusing on NAION?

MR. ALTMAN: I have an objection, Your Honor. Just -- she asked Dr. Blume what was the basis of her, you know, opinion in 2000. I don't know that Dr. Blume has completed her answer. And several times Ms. Leskin has asked her additional questions and interrupted. I think she should have a chance to finish her answer to that question, because it was a pretty broad question, and then when she's

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done with that, I think she can follow up with whatever she wants.

JUDGE BORG: Well, I -- I understand what you're saying. And that's a fair comment. I guess my assumption has been, when it's followed up with another question, that it essentially withdraws the earlier one. But perhaps I'm incorrect -- incorrect in making that assumption.

MS. LESKIN: Well --

JUDGE BORG: Is that -- Ms. Leskin, you did ask a question, and then you stopped it and started with another one.

MS. LESKIN: Right. And --

JUDGE BORG: Do you want an answer to the first one?

MS. LESKIN: Well, I want to under -- I'd like an answer to the second question. And that will help me understand her answer to the first question.

JUDGE BORG: All right.

MS. LESKIN: Because apparent -- what -- what it's telling me is that my question was vague. And I want to make sure we're talking on the same page.

JUDGE BORG: Okay.

MS. LESKIN: So I'm trying to understand her opinion before I go back and let her explain the

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basis for that.

MR. ALTMAN: My only point, then maybe she should withdraw the other question, because I don't think it's --

MS. LESKIN: Withdraw the other question.

MR. ALTMAN: I don't think it's fair that --

JUDGE BORG: It's withdrawn.

MS. LESKIN: I'll withdraw the other question.

BY MS. LESKIN:

Q. So let me just go back to my question.

Is your -- is your opinion here focused on NAION or is your opinion focused on blindness?

A. It's really -- it's focused on both. And the reason is, NAION isn't a term.. So we can't just restrict it to NAION because that's -- that's hiding the ball. Even today the term is ION in the adverse event database. So if we restrict our -- restrict our study just to NAION, we're doing nothing but diluting the numbers even further. And in the periodic safety update reports, it all funnels into optic neuritis.

So what I tried to do in here was to use the terms that your client used at various points in time, recognizing that within optic neuritis we will have NAION reports. And I tried to then look at ones that looked at blindness, since the concern with NAION is the

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blind -- permanent blindness. But it's hiding the ball, Ms. Leskin, to say -- to look only at the term NAION.
Q. Well, I'll give you the term ION. I'm trying to figure out --
A. But, Ms. Leskin --
Q. I'm sorry. There's no question pending.
A. But I have to correct that, because it all codes to optic neuritis --
MS. LESKIN: Move to strike.
THE WITNESS: -- in your client's safety update reports.
MS. LESKIN: Move to strike.
JUDGE BORG: Well, that's not available to you. If you have a --
MS. LESKIN: Okay. Objection; nonresponsive.
JUDGE BORG: Okay. That's sustained.
BY MS. LESKIN:
Q. Is it your opinion that all cases of blindness that are reported are the same as all cases of ischemic optic neuropathy?
A. Well, blindness can come from a variety of reasons. I did not look at blindness that came as a result of a car accident, if that's what you're asking. I was not looking at accidental blindnesses.
Q. Well, can you tell from these -- if something

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is coded to blindness, can you tell if it comes from an accident unless you look at the underlying MedWatch report?
A. Well, luckily with your client's periodic safety update reports, they outline those types of issues. So that's what I looked at with your periodic safety updates, and learned that there were nonaccident events of permanent blindness were coded as early as safety update No. 2. But one has to look at that because you code everything to optic neuritis.
Q. Is there a code for nonarteritic ischemic optic neuropathy?
A. Well, according to what are in your periodic safety update reports, it quotes nonarteritic anterior optic -- nonarteritic anterior ischemic optic neuropathy codes to optic neuritis. So the code is to optic neuritis, but within the safety update reports blindness is discussed separately. And by safety update No. 2, reports of blindness are in the safety updates.
Q. Are you familiar --
A. Nonaccident safety -- nonaccident blindness.
Q. Are you completed your answer?
A. I think so.
Q. Are you familiar with the WHO-ART terms?
A. Yes.

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Q. Are you -- do you know whether there is a WHO-ART term for nonarteritic anterior ischemic optic neuropathy?
A. In what year?
Q. The date --
A. I know it changed over years. So what year it refers -- are you referring to?
Q. The year that you're looking in the periodic safety updates.
A. No, not in the early years. These go back to 1998.
Q. Are you familiar with the MedDRA data -- libraries?
A. Yes.
Q. And are you -- do you know whether there is a term for nonarteritic anterior ischemic optic neuropathy in the MedDRA library?
A. It refers to ION. Codes to ION.
Q. So Pfizer could not have coded to nonarteritic anterior ischemic optic neuropathy under either of those libraries, correct?
A. Well, FDA instruction code to ION. So it would have been coded under ION.
Q. Today?
A.. No, I don't know -- yeah. Back then, too.

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Q. Well, at some point in time, FDA switched from WHO-ART to MedDRA, correct?
A. Yeah. But these all represent codes to ION.
Q. Okay. So Pfizer could not have coded to nonarteritic anterior ischemic optic neuropathy?
A. Correct.
Q. Okay.
A. But that isn't what I was discussing.
Q. That's my question, though.
So let's go back to where we started this afternoon.
When I asked you whether there was a signal, and you told me that there was a signal in 2000 --
A. Uh-huh, in the AERS database.
Q. -- is that a signal for blindness or is that a signal for ION?
A. It's a signal for ION, which was not in the labeling.
Q. Putting aside --
MS. LESKIN: Objection; nonresponsive.
JUDGE BORG: Are you waiting for a ruling? That's sustained.
BY MS. LESKIN:
Q. Putting aside the chart you received from Mr. Altman after you completed your report, please

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identify for me the basis of your opinion as to the signal -- the existence of a signal in 2000 for ION.
A. Okay. The basis for my opinion is that there were reports of permanent blindness in your database beginning with safety update No. 2. And by safety update No. 4, we had -- you had positive rechallenges with blindness. There were also, in peer-reviewed literature, reports appearing in 2000. Those two issues alone would have formed a signal.
Q. So is it your opinion, as I understand today, that the reports in the safety updates that you reviewed, of permanent blindness, would have created a signal for ischemic optic neuropathy?
A. It would have given a signal that the labeling should include that there is potential for permanent blindness, and that that had been confirmed by rechallenge.
Q. Okay. I asked you whether in 2000 there was a signal for blindness or for ischemic optic neuropathy, and you told me that there was a signal for ischemic optic neuropathy. So please explain to me how the identification of events of blindness in the periodic safety updates leads to your conclusion that there was a signal for ION in 2000.
A.. I think what I said is, there was a signal for

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blindness in 2000, and that there was a signal based on the information in the -- in the safety update reports, and that there was a signal for ION in the AERS database.
Q. Okay. But as of the time you prepared your report, you did not have the information from the AERS database, correct?
A. Right, which is why I use blindness into my report..
Q. Okay. So you've supplemented your opinion. Is that fair to say?
A. Well, my concern is that permanent blindness get in there. Now -- yeah, I guess that is additional information. But the point is, permanent blindness needed --
The reason we're concerned with ION is the end result of permanent blindness. Permanent blindness was known to you early after the market launch. The fact that we now know that there are also specific terms coded to ION and now NAION, all is permanent blindness..
Q. Doctor, if blindness is due to glaucoma, does that help a patient know about ischemic optic neuropathy?
A. Well, your -- your safety updates differentiated between blindness and that related to

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glaucoma.
MS. LESKIN: Move to -- objection; nonresponsive.
JUDGE BORG: Sustained.
Doctor, did -- do you understand her question?
THE WITNESS: No.
JUDGE BORG: Okay. You know, if you don't, would you please tell her that so she can rephrase it?
THE WITNESS: Yes.
JUDGE BORG: Thank you.
MS. LESKIN: Thank you.
JUDGE BORG: Ms. Leskin, you want to try again?
MS. LESKIN: I will try again.
BY MS. LESKIN:
Q. Is blindness due to glaucoma the same as blindness due to ischemic optic neuropathy?
A. No.
Q. Would warning a patient about blindness due to glaucoma -- strike that.
MR. OVERHOLTZ: Yeah, it sure would. It'd keep them from prescribing it.
THE WITNESS: Yeah.
MR. OVERHOLTZ: Keep them from going blind.
MS. LESKIN: I'm sorry. Are you testifying

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here, Mr. Overholtz?
JUDGE BORG: Oh, come on, let's -- let's --
MS. LESKIN: Well, I'm tired of being interrupted.
JUDGE BORG: Yeah, I understand that.
MR. BECNEL: How can we interrupt you when you've got an outline of what you're doing.
JUDGE BORG: You know, guys, that -- that has no place in the record, and it -- and it has no place between professionals.
Ms. Leskin, proceed, please.
MS. LESKIN: Thank you.
BY MS. LESKIN:
Q. What would you recommend -- what would --
In your opinion, what should the label have been changed to include in 2000?
A. Oh, I think in 2000 the post-marketing adverse events should have included that reports of blindness, permanent blindness, and ION had been received, and that rechallenge -- that there was positive rechallenge information in the -- in patients who had received Viagra on multiple occasions and had suffered visual loss. And, I mean, at a minimum it should have gone into the post-marketing adverse events information.
Q. What's the basis for that opinion, the

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regulatory basis for that opinion?
A. Well, post-marketing adverse events are -- are to be included when there is -- based on a variety of categories, but certainly one of them is seriousness.
Q. Is it your testimony that every time a company gets adverse event, it needs to be included in its label?
A. No, and nor did I say that.
Q. I want to make sure.
A. But this one is a recreational drug and results in permanent blindness, so that fits the category of what should go into a post-marketing adverse event --
MS. LESKIN: Objection.
THE WITNESS: -- section.
MS. LESKIN: Objection; nonresponsive.
JUDGE BORG: Sustained.
I -- you know, Doctor, I know you're frustrated by this and -- I mean, at least it's clear to me that you are. Sort of the rules of the road when we do these depositions is that she does get to control your answers to an extent. I know you have more information that you would like to offer that you think will clarify it. Mr. Overholtz, Mr. Altman, Mr. Becnel have an opportunity to do that if they think it's necessary for the record.

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THE WITNESS: But, Judge, I understand how it works, but I am trying --
JUDGE BORG: I know that you do.
THE WITNESS: -- to answer these questions.
And it's this parsing of critical information in an effort to dilute and demean and denigrate clearly available information that should have been included in a labeling. There is no -- no confusion --
JUDGE BORG: I -- I understand --
THE WITNESS: -- it should have been in the labeling.
JUDGE BORG: I understand your frustration with her parsing it out. She gets to do that.
THE WITNESS: Oh, I -- No, I understand. I've done this --
JUDGE BORG: Okay.
THE WITNESS: -- before, but --
JUDGE BORG: Well, I understand that you have. So have I. And I'm just trying to get some rules of the road here because it will go faster for everybody, it will go more smoothly.
MS. LESKIN: I'm going to mark as Exhibit 8, October 10, 2000, "Sildenafil: Glaucoma, Increased Intraocular Pressure, Retinal Detachment, Retinal

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Hemorrhage, and Blindness," a report prepared by Pfizer.
(Exhibit No.. 8 was marked for identification.)
BY MS. LESKIN:
Q. You've seen this document before, haven't you?
A. I think so.
Q. Turn with me to page 8. And that's the section on blindness that you're referring to, right?
A. Well, I was referring to the safety update report. This is not the safety update report.
Q. Okay. You're right.
But this is a discussion, a review of the cases of blindness as of 2000, correct?
MR. OVERHOLTZ: Object to form; lack of foundation.
THE WITNESS: Just one second.
JUDGE BORG: Can you lay some more foundation, Ms. Leskin?
MR. OVERHOLTZ: I don't think she can. But I don't think the witness can ever know what this is.
JUDGE BORG: Well --
THE WITNESS: Well, I do know that it -- I'm sorry.
JUDGE BORG: No, no. That's all right.
Are you able to identify it?

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THE WITNESS: Well, it's not the safety update. And it also cut off in August of 2000. So it's not the end of 2000, this report.
BY MS. LESKIN:
Q. I'm sorry. I didn't realize I said end of 2000. As of 2000. But to be more specific, I'll rephrase my question.
This is a discussion of the review of cases of blindness as of August 2000, correct?
A. Yeah, among other things, yes.
Q. This section that I referred you to refers to blindness, correct?
A. Oh.
Q. On page 8?
A. I'm there.
Q. Okay. Now, four of the cases of blindness, if you look at the second paragraph on that section, the physician denied ever reporting them, correct?
A. I'm sorry. Where are you now?
Q. The second paragraph under blindness.
JUDGE BORG: Page?
MS. LESKIN: Page 8.
BY MS. LESKIN:
Q. Do you see that?
A. Yes.

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Q. But those four reports don't go away, correct?
A. No.
Q. They remain in the database, correct?
A. I would hope so.
Q. And they would add to the numbers that you saw in the AERS database, correct?
A. They could.
Q. Well, they do, don't they?
A. Yep.
Q. Then there's another case that talks about temporary blindness of less than a minute, right? That's the next case in the list, same paragraph.
A. Yes.
Q. And that physician said the patient didn't even take sildenafil at the time of the event, right?
A. Yes, you've read it correctly.
Q. But that report stays in the database, correct?
A. It's required to, yes, unless they show that it's a duplicate.
Q. And that shows up in the counts that you have looked at, correct?
MR. ALTMAN: Objection; misstates -- misstates her testimony.
THE WITNESS: Yeah. And I have no idea if this was one of the ones.

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JUDGE BORG: It's overruled. Your witness has answered the question.
MR. ALTMAN: Got to wait for an objection.
THE WITNESS: Oh, I'm sorry.
BY MS. LESKIN:
Q. Now, you also referred to the incidents of rechallenge. You told me that we had -- one of the bases for the -- one of the bases for your opinion that there was a signal is because there was evidence of a rechallenge of blindness in this case in this report. And that's what you referred to on page 28 of your report, correct? In fact you wrote, "A positive rechallenge was reported in one case of a 28-year-old male experiencing temporary blindness on three separate occasions."
A. Yeah, I assume that's the same three patients -- three --
Q. Well, that's in fact the Bates number?
A. Bates number, yeah, it is.
Q. Now, this is the document you're citing, correct, not the safety update?
A. No. I cited a separate number. So it wasn't the safety update.
Q. You cited the document that we've marked here as Exhibit 8?

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A. 03283827 -- yes.
Q. That was temporary blindness, correct?
A. Yes, three times.
Q. Do you know if that's at all related to ischemic optic neuropathy?
A. Temporary blindness? I think it can be.
Q. Do you know if the temporary blindness that this 28-year-old patient reported was related to ischemic optic neuropathy?
A. No. The point of it is that it was a positive rechallenge, which is a safety signal.
Q. For ischemic optic neuropathy?
A. No, for blindness, in that it was related to the drug.
Q. Doctor, the concern -- the confusion I'm experiencing here -- and maybe you can help me -- is I keep asking about a signal for -- in 2000, and you told me at some point that the signal was for ischemic optic neuropathy, in 2000.
And so the basis for that signal that -- for ischemic optic neuropathy in 2000, is that solely the AERS database or is that these reports of temporary blindness that may or may not be ischemic optic neuropathy?
A. Well, I think there's two opinions. Ischemic

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optic neuropathy is certainly confirmed by the AERS database. The fact that there was blindness, reports of blindness, permanent blindness, and ischemic optic neuropathy occurred in the safety updates as well; and that there was permanent blindness in those reports in 2000, 2001, and 2002. So in both instances there were permanent blindness reports and then ischemic optic neuropathy, and neither of them were in the labeling.
Q. And you're not distinguishing in your mind between blindness and ischemic optic neuropathy when you're doing this analysis?
A. I am. But because they all coded to optic neuritis, I was particularly interested in the blindness.
Q. But --
A. Everything -- everything filters to one bucket with this optic neuritis. So rather than just look at the bucket, which is not the fair way of doing it, but would have been even bigger numbers, I looked at those events of interest, which were the blindness and ION, if it was reported that way. But that was oftentimes hard to tell because it all coded to optic neuritis.
So my concern is that physicians and prescribers know, patients know that it can cause permanent blindness. And when we had more information

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about ION and then NAION, that that information be added to the database. So it is a continuum that needed to be done.

(Exhibit No. 9 was marked for identification.)

BY MS. LESKIN:

Q. Let me show you what we've marked as Exhibit No. 9. This is a letter from Dr. Richard Siegel to the editor of the Ocular Surgery News.

You've seen this document before, haven't you, Doctor?

A. Yes.

Q. You cite that in your report, correct?

A. I don't -- I don't recall the specific page. Let me look.

I'm sorry. Can you direct me to the page I cite it?

Q. Uh-huh. If you look at page 13.

A. Yes.

Q. First paragraph, you have the sentence: "While Pfizer was aware of these NAION cases in 2000, their response seemed to focus on deflecting the negative publicity which they knew would result rather than initiating an update to the product labeling or performance of the necessary epidemiologic study required to determine the relatedness of this adverse

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event to the drug's use."

Do you see that sentence?

A. I do.

Q. And you see up in the middle of that sentence, you cite three different Bates numbers or Bates ranges?

A. Yes.

Q. Do you see that middle number --

A. I do.

Q. -- 003 --

A. I see it.

Q. -- 085962?

A. I see it.

Q. That's Exhibit 9, correct? The Bates number matches?

A. Yes.

Q. Okay. So you've looked at this letter before, correct?

A. Yes.

Q. Do you know of the circumstances under which this letter was written?

A. I recall that there had been a release, and they were referring -- responding to a lease -- release.

Q. By whom?

A. A release -- I -- I think it's the original work with Pomeranz, Dr. Pomeranz.

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Q. Looking at that, I guess the bottom paragraph that starts, "With regard to the letter by Dr. Pomeranz..." Do you see that? Do you see where I am, about halfway through the letter?

A. Yes.

Q. It says, "...we have conducted a review of Pfizer's worldwide clinical trial and post-marketing spontaneous adverse event reporting database covering multiple 'optic nerve' reporting terms."

JUDGE BORG: Ms.. Court Reporter, are you getting all that?

MS. LESKIN: I'll start that again.

BY MS. LESKIN:

Q. The sentence reads: "With regard to the letter by Dr. Pomeranz, we have conducted a review of Pfizer's worldwide clinical trial and post-marketing spontaneous adverse event reporting database covering multiple 'optic nerve' reporting terms."

Do you see that sentence?

A. Yes.

Q. Okay. Do you have any reason to believe that Pfizer did not in fact do that review?

A. No.

Q. "To date, there are over 11,000 person year of exposure to sildenafil in our controlled clinical

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trials."

Do you see that sentence?

A.. Yes.

Q. Do you have any reason to doubt the truth of that statement?

A. I -- I have never argued that they did not see this in a -- in the NDA program.

Q. Okay. So -- but that's a correct number, right, that as of 2000 there were over 11,000 person-years of exposure to sildenafil, correct?

A. Well, no. There were -- they're referring to their controlled clinical trials with that number.

Q. Correct. And they had 11,000 person-years of exposure in the controlled clinical trials, correct?

A. That's what it says. I mean, I have -- I have no way of calculating that number, but that's what they say.

Q. You have no basis to disagree with that number, though, right?

A. Or agree with it.

Q. Okay.

A. I don't know.

Q. "There have been no cases of anterior ischemic optic neuropathy reported among these patients."

You have no reason to disagree with that,

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correct?
A. Right. In the controlled clinical trials, right.
Q. Correct.
"With approximately 30 million prescriptions for sildenafil having been written worldwide since its U.S. approval in March 1998, representing approximately 250 million tablets dispensed, the case reported by Drs. Egan and Pomeranz is the first well-documented case of AION with a possible temporal relationship between sildenafil intake and onset of the event."
Is that a true statement?
A. I don't know how many other events there are. They're saying that that's the first event where there has been all three criteria, first documented case of ION that had a documented temporal relationship and had a relationship between the intake and the onset of the event. I don't know what they mean by that, if that's the first ION event or if that's the first that they know of that complied with all three of their conditions, and that there are others. I don't know the answer to that.
Q. So you don't know whether that's a true statement or not?
A. I don't know if there's others that don't

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comply with the three criteria Pfizer laid out.
Q. "We currently do not have any detailed information on the other cases mentioned in the Pomeranz letter."
Do you know what other cases he's talking about?
A. No.
Q. "Any future discussion about AION and sildenafil must take several facts into account: the age range of patients who spontaneously develop AION and those taking sildenafil appear to overlap."
Is that a true statement?
A. Well, if he is saying that ION more likely in middle-aged people, middle-aged men, I guess that's true.
Q. It says, "Although this apparently did not apply to the patient reported, sildenafil is most often taken in the evening, and there's a well-described temporal association of spontaneous AION, which occurs most often during sleep."
Are you aware of that statement?
A. Yeah. I have seen Dr. Hayreh's, yes.
Q. It says, "Based on the above, at present we do not believe that the events reported by Drs. Egan and Pomeranz represent evidence of a problem with

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sildenafil."
Is it your opinion that as of June of 2000 that that was an incorrect statement?
A. "We do not believe -- represent" --
I believe it represents evidence that it needed to be in the labeling, and that prescribers and patients should decide if that was a problem with sildenafil.
Q. And then he says, "We will continue to follow with care the information being collected by Drs. Egan and Pomeranz."
That is a responsible thing to do, correct?
A. Well, it's -- it's required.
Q. And the FDA was aware of the event published by Dr. Pomeranz, correct?
A. Yes.
Q. In 2000, did the FDA request Pfizer to change its label to include ischemic optic neuropathy?
A. I don't know. It's not the FDA's job to do that. It's the -- it's the company's job. The company knows more about their product than anyone else.
MS. LESKIN: Objection; nonresponsive.
JUDGE BORG: Sustained.
BY MS. LESKIN:
Q. Doctor, did the FDA request Pfizer to change its label in 2000 to include ischemic optic neuropathy?

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MR. OVERHOLTZ: Objection; lack of foundation. There's no foundation that the FDA is the one to request Pfizer change its label.
JUDGE BORG: Let's hear the question again.
BY MS. LESKIN:
Q. In 2000, did the FDA request Pfizer to change its label to include ischemic optic neuropathy?
JUDGE BORG: If you know.
THE WITNESS: I don't know. And FDA did not have the authority to require that until 2008.
JUDGE BORG: The question -- the answer was: "I don't know."
BY MS. LESKIN:
Q. In 2000, the FDA could have requested that Pfizer change its label to include ischemic optic neuropathy, correct?
A. Yeah, I guess it's possible..
Q. And you've looked through all of the documents that have been produced in this litigation. Did you find any evidence that the FDA, in 2000, requested that Pfizer include ischemic optic neuropathy in its label?
MR. ALTMAN: Objection.
MR. OVERHOLTZ: Objection.
MR. ALTMAN: Misstates the testimony.
MR. OVERHOLTZ: Lack of foundation.

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JUDGE BORG: It's -- let me hear the question again.
BY MS. LESKIN:
Q. You've looked through all the documents that have been produced in this litigation. Did you find any evidence that the FDA, in 2000, requested that Pfizer include ischemic optic neuropathy in its label?
JUDGE BORG: Overruled.
MR. OVERHOLTZ: Well, it -- it's --
MS. LESKIN: You've made your objection. It's been overruled.
MR. ALTMAN: Your Honor.
JUDGE BORG: Are you able -- do you understand the question?
THE WITNESS: I thought I answered it. I don't know..
JUDGE BORG: Okay.
BY MS. LESKIN:
Q. You don't know if you found any evidence?
JUDGE BORG: Well, hang on a second, Ms. Leskin.
What's the problem, Mr. Altman?
MR. ALTMAN: Only to the extent she said, "You looked through all of the documents that have been produced." She never said she looked through every

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document in the litigation.
JUDGE BORG: Well, she answered the question "I don't know" anyway, but --
MR. BECNEL: Judge, as you know, the authority of the Congress to give the FDA authority to require label change only occurred just a few days ago. Prior to that, they didn't have any authority to do it.
THE WITNESS: That's right.
MS. LESKIN: She's testified that they had the authority to request.
MR. ALTMAN: I'm -- I'm just trying to address the one issue. She said, "You reviewed all" --
JUDGE BORG: I understand. But the answer got rid of it anyway.
MR. ALTMAN: Okay.
JUDGE BORG: Because she said, "I don't -- I don't know."
MR. ALTMAN: Okay.
JUDGE BORG: I understand your objection, though.
Ms. Leskin, go ahead.
BY MS. LESKIN:
Q. You don't know if you found evidence or not?
A. I don't know if they asked the -- I didn't -- I

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didn't see any evidence. But I don't know if they asked them.
Q. But you didn't see any evidence of that?
A. No. And more -- no, I didn't see any evidence.
Q. Did you see any evidence that Pfizer -- that --
Did you see any evidence that the FDA requested Pfizer to change its label to include ischemic optic neuropathy at any time prior to 2005?
A. Did you say FDA or regulatory authorities?
Q. FDA.
A. No. I -- no, I didn't see any evidence that FDA asked them prior to 2005.
Q. One of the things we spoke about earlier that a company can do to investigate a safety signal is to look at animal studies, correct?
A. Well, I agreed that that could be done, yes.
Q. Are you aware of any animal studies that Pfizer conducted on -- that would -- strike that.
Are you aware of any animal studies that Pfizer conducted for Viagra?
A. I'm aware of the ones that were submitted in the NDA.
Q.. Do you know how, if at all, those studies would impact Viagra's effect on vision?
A. No. How the -- which animal model -- to what

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are you referring?
Q. Any animal model.
A. No, I don't think there's an animal model that's directly applicable to human ION or NAION.
Q. Okay. My question was a little broader than that for this time.
My question said: Do you know how, if at all, that the studies that Pfizer did do can measure Viagra's effect on vision?
A. In animals?
Q. In animals.
A. No.
Q. If you can pull out Exhibit 5. Just a visual summary.
MR. BECNEL: Which page?
MS. LESKIN: I haven't directed her to a page yet.
MR. BECNEL: Oh.
BY MS. LESKIN:
Q. If you look at page 15, section 6, entitled "Summary of Preclinical Visual Study -- Findings."
Have you reviewed this information before?
A. Yes, I've seen it before.
Q. Okay. And the first paragraph talks about the effect on PDE6, correct?

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A. Yes.
Q. Second paragraph says, "In toxicology studies, administering doses in excess of those shown to be pharmacologically active in the retina, daily for up to 24 months, does not result in any treatment-related toxicity of the retina or eye."
Were you aware that those studies had been done?
A. Well, they're required to be done.
Q. Were you aware they had in fact been done?
A. Well, the FDA approved the NDA so, yes, they had to be done, and they were done.
Q. And if you look at the section above that, it's part of a section called "Histology." Do you see where I'm directing you?
A. Yes.
Q. And if you look at the first -- top paragraph on page 15, they found no statistically significant difference in the number of nuclear layers of the retina following high doses of Viagra, correct?
A. Yes.
Q. Were you aware those studies had been done?
A. Yes.
Q. And if you look at the paragraph below that, it says that there were no evidence of an effect on the

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treatment of the -- on the retina, tapetum in dogs, choroid or associated blood vessels in the animals tested..
Do you see that?
A. Right. The animal models did not show any perturbation of retinal function, so they didn't serve as a model for what was seen, even with the blue-green tinges, seen in humans. So as I said, there is no animal model that would reflect this. And indeed Pfizer's own animal database didn't reflect what they saw with the blue-green tinges and the changes in the retinal blue-green perception. So the animal models were not predictive at all, even for the retinal changes that were observed with the blue-green tinges.
Q. Are you aware -- familiar with the Bernstein model for NAION that's been developed?
A. No. Bernstein animal model?
Q. Yes, of rats.
A. The rat model. I think I did see that, but I'm not -- I'm not an expert in that at all.
Q. Okay. And Dr. -- are you familiar that Dr. -- well, you said you saw that.
Are you aware that Dr. Bernstein used a laser-activated dye to ablate the blood supply to the optic nerve in rats as part of that model?

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A. I think I looked it over, but I don't recall.
JUDGE BORG: Five minutes.
BY MS. LESKIN:
Q. Now, you'll agree with me that that's not a valid model to assess the impact of a drug in causing NAION, right?
A. I don't know if any model will work. I mean, the rat models didn't work, didn't -- didn't predict a change in humans. And I don't know if the Bernstein model's been accepted for humans. I don't -- I don't know. But it wasn't an issue at the time the product was approved.
Q. Well, was it at issue at any time after the product was approved?
A. Well, I mean, I guess they could have done the studies, but they already knew that the animal models were not predicting. And in any event, animal models never trump human experience. One does not avoid addressing human safety issues because of negative animal models. Clinical data are always the most important.
Q. But animal models are useful to understand whether there is in fact a cause and effect relationship between a drug and an event, correct?
A. You -- well, you can -- you can't -- I mean,

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it -- no. There's three ways of looking at causation in humans. And, again, causation is not an issue for what I'm talking about because causation does not impact whether one puts information in their labeling.
Q. Do you believe that you should put information in your labeling that doesn't have any scientific basis?
A. No.
Q. If there was a report of an adverse event that occurred, but investigation demonstrated that it was not -- definitively that it was not related to the event, should that event show up on the label?
A. Can you give me more information about the event? I'm not sure what you're talking about.
Q. Sure. Well, if there's an adverse event reported, but evidence is clear that there is no causal relationship, should that adverse event show up on your -- on your label?
A. How was that causality issue determined?
Q. However it was determined, you were able to definitively say. You can't answer?
A. I can't answer a question like that. I mean, there are times when one adverse event would be enough to put it in the label.
JUDGE BORG: Let's break.
MS. LESKIN: Yep.

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THE VIDEOGRAPHER: We're off the video record.
(Recess from 2:05 p.m. until 2:24 p.m.)
THE VIDEOGRAPHER: We are back on the video record.
BY MS. LESKIN:
Q. Dr. Blume, you have this chart here, that you've been referring to, based on the numbers that Mr. Altman provided you. Can we mark that as an exhibit to this deposition? I'm going to ask you to put No. 10 on the bottom there.
(Exhibit No. 10 was marked for identification.)
MR. BECNEL: Have you got a duplicate of that or is that the only one?
MS. LESKIN: That's the only copy, as far as I know.
MR. BECNEL: We're going to have to make some copies of that.
MS. LESKIN: We'll get them with the -- when the court reporter circulates the transcript. That's fine. It's okay.
THE WITNESS: I'll make copies at a break. I'll make a copy at the next break.
MS. LESKIN: Do that, too.
BY MS. LESKIN:
Q. The numbers that are on there, are those

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cumulative numbers or annual numbers?
A. Yes, that's what I indicated, they're cumulative.
Q. They are cumulative. Okay.
Do you know the total number of adverse events reported for amiodarone, all events, over that time period of 1998 to 2004?
A. For -- adverse events for ION.
Q. No, all adverse events for amiodarone.
A. No.
Q. How about interferon, do you know the total number of all adverse events reported over the time period 1998 to 2004?
A. No.
Q. And the number of ION events that are on that list that you have in front of you, Exhibit 10, you don't know what percentage of adverse events for amiodarone that number represents, correct?
A. No. I would not have been interested in that for this, no.
Q. And you don't know the percentage of adverse events for interferon that the -- that the ION number on your chart there represents, correct?
A. No. It did not have relevance as to the data mining that I was doing.

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Q. Okay.. What authority are you relying on for that chart to show that that is an acceptable way to determine whether there's a safety signal?
A. The use of the AERS database?
Q. In the method in which it's presented on Exhibit 10.
A. Well, the AERS database of course is -- is a product of the FDA and acknowledged by the FDA and required by FDA as part of your safety surveillance techniques. And it -- this is the most conservative approach of this because it does -- it narrows it to the serious and suspect events rather than taking all events. So this represents the most conservative way of looking at the data. The numbers would have been larger, not limited to serious and suspect.
And as far as looking across different drugs and looking for a signal, it's commonly done by FDA. If you look at FDA's example of the publication that FDA did when they instructed Bayer to remove Baycol from the marketplace, it was because they compared Baycol's adverse events relating to rhabdomyolysis with those of other statins.
Q. Is amiodarone in the same class as Viagra?
A. No.. Amiodarone is Cordarone. It's a cardiovascular product.

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Q. So it's not in the same class as amiodarone, correct -- I mean as Viagra, correct?
A. No. It's a cardiovascular product.
Q. Is it a phosphodiesterase type 5 inhibitor?
A. I -- I doubt it. No, I don't think so.
Q. Is interferon in the same pharmaceutical class as Viagra?
A. No.
Q.. Is Vioxx in the same pharmaceutical class as Viagra?
A. No. Vioxx is a COX-2 inhibitor.
Q. And interferon also is not a phosphodiesterase type 5 inhibitor, correct?
A. Correct, right.
Now, when the other products were approved, that are sister drugs to Viagra, it would be appropriate to include those on this list as well. So if we were looking at after 2002 and 2005, we would -- we could include the other drugs as well.
Q. And you haven't done that analysis, correct?
A. I don't -- no, I did not.
Q. If you could turn with me to page 13 of your report.
A. Can I make a clarification?
Q. Okay.

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A. I think I said earlier that these reports were coded as ION. And I wanted to clarify that these reports come from the company's database. So these would have been coded as ION by the company. I don't know if I made that point clear before. I think I might have complicated that unnecessarily. This is the adverse event database, so they would have been coded by the company as ION.

Q. I'm on page 13 of your expert report, please. Are you there with me? Are you there with me?

A. Oh, yes.

Q. Okay. That first full paragraph starts with the sentence, "While Pfizer was aware of these NAION cases in 2000, their response seemed to focus on deflecting the negative publicity which they knew would result rather than initiating an update to the product labeling or performance of the necessary epidemiologic study required to determine the relatedness of this adverse event to the drug's use."

Do you see that sentence?

A. Yes.

Q. Is this sentence part of your opinion held to a reasonable degree of scientific certainty?

A. Well, we know that Pfizer -- I would say yes, because Pfizer, we know it was aware of ION cases. They

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coded them as such. They had a signal in 2000 from this publication, and their commitment to track it in 2000. So they were certainly aware of this. And I did not find any effort in 2000 to update the product labeling. And I believe that you indicated earlier that the epidemiologic study was not started by Pfizer until several years later, I think in 2007.

MS. LESKIN: Objection; nonresponsive.

JUDGE BORG: Sustained.

BY MS. LESKIN:

Q. The question, Doctor, was: Is this sentence part of your opinion held to a reasonable degree of scientific certainty?

A. Well, I thought I answered yes and then explained why.

Q. Okay. But, yes, it is held to a reasonable degree of scientific certainty?

A. Yes.

Q. What science did you use in applying -- what science did you apply in reaching this opinion?

A. Well, I tracked to see if they were aware of these databases. And as I just indicated, they coded them this way for FDA purposes. They said that they were aware of ION and promised to track it. I believe there is a follow-up -- there is an e-mail from

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Dr. Siegel in the database where he is talking about needing to follow up on this, and perhaps connecting with Dr. Hayreh for this. So they were certainly aware of it and had promised to follow up on it. So I tracked what the company was doing internally.

And then I tracked the labeling chronologies to see if there was any labeling submissions in 2000 to add blindness, ION, or NAION, and could not find any, and did not find any labeling changes relating to those.

And I relied upon Pfizer's statements through 2005 and 2006 that they could not do an epidemiology study, did not believe one could be done, and then relied upon their commitment to do one after FDA insisted and the notice in the FDA website that it was starting in 2007.

Q. What science -- what branch of science is that?

A. It's regulatory affairs.

Q. And you're selling -- you're telling this --

You're telling us that you used a -- the science of regulatory affairs to conduct that -- that analysis?

A. It's standard regulatory and pharmacovigilance behavior for a pharmaceutical company. I'm -- I'm not sure what you're meaning by science. Such as anatomy or physiology? I don't know what science would come into

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that sentence, other than collection of the normal information that a drug company collects.

Q. What's the basis for the part of the opinion where you said, "Their response seemed to focus on defecting the negative publicity"?

A. I was aware of information that they were going -- that they were going to use in discussing the Egan and Pomeranz information, and it was directed to the field staff on how to answer the question if this was an issue, if the question was raised to them by any of their practitioners. And those answers did not include that a study was going to be -- an epidemiology study was going to be done, but rather it talked about issues such as this is the normal age of patients where this occurs.

We didn't see any in our clinical trial data. Pfizer didn't see any in their clinical trial data. The incidence rate isn't even as high as what normally occurs as back -- as background incidence of this..

So it appears that their concern was diluting the consequences of the Egan finding rather than discussing the potential for vision loss as it agreed -- as it -- as it was at that point in time with prescribers.

Q. I want you to take a look at the document that

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we identified before, the letter by Dr. Siegel, which would be to Ocular News Surgery. Do you have that in front of you?
A. Are you referring to Exhibit 9?
Q. Yes. Yes.
A. Then I have it.
Q. Okay. Where in that letter does it say anything about deflecting negative publicity?
A. It doesn't.
Q. That's just your --
A. I doubt if it --
Q. -- interpretation?
A. I doubt if it would say that in a -- in a response letter to an outlet.
Q. So is that just your interpretation of the letter?
A. Of that letter? No. It's my interpretation of all the documents that I just mentioned. And in fact --
Q. Okay. Well, let me -- I'm just talking about this letter right now. If you look at that sentence on page 13 that we just read, you cite three documents, correct? You cite --
A. Yes.
Q. Okay. And that's -- Exhibit No. 9 is the second document, right?

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A. Yes.
Q. Okay. So are you relying on that letter as support for your statement that Pfizer's response seemed to focus on deflecting the negative publicity which they would -- which they knew would result?
A. Well, I think -- well, yeah, let's look at this. This is June of 2000. And they're saying this is the first event that they have, but yet ION -- target -- ION coded events had already been submitted to the AERS database. So I'm not sure where that statement comes from, unless it is because they have applied these three criteria along with that statement.
And they also are saying that they had patient populations, none in their clinical trials, but we know their clinical trials was a selected group to exclude some of the other risk factors. They also say that it's the only one meeting those criteria. They conclude that they don't believe they have a problem, and that they promise that they will follow up.
So, yeah, I think it -- I think it is an example of diluting the importance of the findings.
MS. LESKIN: Objection to everything except the last sentence of that answer --
JUDGE BORG: It's overruled.
MS. LESKIN: -- as nonresponsive.

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JUDGE BORG: It's overruled. The answer stands.
BY MS. LESKIN:
Q. Where in that letter does it say "deflecting negative publicity," Doctor?
A. Oh, it doesn't.
Q. That's your interpretation of the letter, correct?
A. And my paper says, "Their response seemed to focus." I don't have quote marks in that response, nor do I say their response was -- did deflect. I said, "It seemed to focus."
Q. Okay. That's your interpretation of the document, correct?
A. Yes. That's -- well, it's my interpretation of multiple documents, but yes.
Q. Okay. The first document you have listed on that list is 211665, correct?
A. Yes.
Q. I'm going to mark that Exhibit 11.
(Exhibit No. 11 was marked for identification.)
BY MS. LESKIN:
Q. This is a May 23rd, 2000 memo from Shira Rohde to distribution, subject Viagra PNP team meeting of 27 April 2000, right?

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A. Yes.
Q. And is that in fact a document that you refer to on page 13 in that sentence we read -- we just read?
A. I think so.
Q. I'm going to ask you to turn to page 8 of the document..
Well, first, before you get there, can you show me where in that document it refers to deflecting negative publicity?
A. Of course the article, of course it doesn't say they're going to deflect negative publicity, nor did I say they said that. I said it seemed to.
Q. Okay. That's your --
A. And the reason --
Q. That's your interpretation of the document, correct?
A. Well, because of the following: that they say that they think that Dr. Egan is going to begin discussing, that he was going to present his findings to -- at the American Academy meeting. So they -- their response was, they were -- it would be useful to proactively write a manuscript reviewing sildenafil's effects on ocular blood flow.
Q. Doctor, can I ask you to read that sentence in its entirety, please?

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A. Yes. "After the -- after the article was published, Dr. Egan received calls from other ophthalmologists reporting five additional" -- oh, here's another five additional cases of ION.. Oh, in 2000. So that should be added to the tally. I didn't even see that until right now.
Q. Do you know if that's included in the ION -- in the ION database that you have in your chart?
A. I wouldn't be able to tell. This is in May of 2000. I don't -- I don't know by month. I wouldn't be able to tell.
Q. So you --
A. But I have --
Q. So you have no idea whether those numbers need to be added to the tally or not; isn't that true?
A. Well, let's see. Egan and Pomeranz had seven. This is five. And in the safety update reports, there's two others reported. So we're over 12 already, and it's only May of --
Q. I'm sorry.
A. -- two thousand --
Q. Go through that math again for me, Doctor.
A. Well, we had seven with Pomeranz, five more here.
Q. When did you have seven with Pomeranz?

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A. Oh, two thousand -- I don't know if it was two -- maybe 2002. So I don't know. I don't know if they're included. But it's another signal that I did not include in my discussion with you regarding what signals they have.
So now we have AERS is a signal in 2000, Egan in June of 2000. And in fact we learn in May of 2000, there is other cases that were unbeknownst to Dr. Egan. So now we have three different signals by mid 2000.
So anyways, continuing with reading, picking up with the second sentence, "He" -- and I believe that's referring to Dr. Egan -- "is planning to write these up for presentation to the American Academy of Ophthalmologists meeting in the fall. R. Siegel, A. Laties, and I. Osterloh have been discussing whether it would be useful to proactively write a manuscript regarding sildenafil's effects on ocular blood flow."
Q. Reviewing, correct? Isn't that word "reviewing"?
A. Right, reviewing.
Q. What's the action item that came out of that meeting?
A. "McLaughlin is going to contact Egan to get follow-up information on the five new cases of ION."
Q. And that's exactly what the company should be

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doing, correct?
A.. Well, they're required to do that.
Q. So that's what they should be doing, correct?
A. Because they have to do it. They should do it because they're required to do it.
Q. Do you know what information came out of Dr. McLaughlin contacting Dr. Egan?
A. No.
Q. Do you know if Dr. Egan confirmed that he actually had five additional cases?
A. Not Dr. Egan. Dr. Egan is receiving calls from other ophthalmologists who have cases. This isn't Dr. Eagan.
Q. "Dr. McLaughlin will contact Dr. Egan to get follow-up information on the five new cases of ischemic optic neuropathy," correct?
A. "Dr. Egan received calls from other ophthalmologists reporting five additional cases."
Q. Do you know whether --
A. It's other ophthalmologists.
Q. Do you know whether that information actually ever existed?
A. Well, I'm -- I have no reason to believe that Dr. Egan would lie, but I don't know what happened in the follow-up. It's another signal in 2000.

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Q. That requires follow-up by the company, correct?
A. Of course. All signals are required to be followed up. Of course.
Q. And that's exactly what the company did, correct?
A. Well, the company didn't do a study, and the company didn't tell prescribers, and prescribers couldn't tell their patients.
Q. If Dr. McLaughlin had contacted Dr. Egan, and Dr. Egan said, "You know what, it's really not five cases of ION, it's something else," would they still have been required to change the label, if that didn't pan out?
A. Well, yes, if it -- if those cases were blindness. Yes. I'm not -- yes, if it were --
Q. You don't know --
A. -- blindness.
Q. You don't know what those cases were, do you?
A. No. And I don't know -- they may have been permanent blindness. I don't know.
Q. And they may have been --
A. I'm just --
Q. -- nothing, correct?
A. I doubt it, but perhaps.

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And the point is, you asked me earlier what signals there were in 2000, and I was saying I didn't know that there was an additional signal in 2000. So now we're up to at least three.

Q. And all those signals require the company to follow up, correct?

A. The company is required to follow up on signals.

Q. And where in this document does it talk about deflecting negative publicity?

A. Well, I don't know how many ways to answer this for you.

The term "deflecting negative publicity" is mine, and nor did I say they did it. I said it seemed to focus on deflecting it.

Q. And that's your interpretation of this document, correct?

A. Versus who else's?

Q. So that's your interpretation, correct?

A. I don't know to whom else you might be referring. Of course it's mine.

(Exhibit No. 12 was marked for identification.)

BY MS. LESKIN:

Q. I show you Exhibit 12. The document's entitled "Response to Press Release and News Story Regarding

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Viagra and Nonarteritic Anterior Ischemic Optic Neuropathy." And this is the third document that you cite, correct, on this page 13 on that top sentence we've been discussing?

JUDGE BORG: Of exhibit which?

MR. BECNEL: 12. This one.

MS. LESKIN: This is Exhibit 12. We've been discussing page 13 of her report, which was Exhibit 1.

BY MS. LESKIN:

Q. Is this in fact that document?

A. Yes. And I have to correct an earlier answer.

They had -- Pfizer had seven cases of documented ION by January of 2001. I think I earlier said they had five. They had seven, according to this document.

Q. As of January 2001, correct?

A. Yes.

Q. Okay. Show me where in this document it refers to deflecting negative publicity.

A. I'm sorry. Are you waiting for me to answer?

Q. Yes. My question was: Show me where in this document refers to deflecting negative publicity.

A. Well, it's the same answer I gave you before. These are documents relating to Pfizer's opinions. I'm

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pretty confident they're not going to say, "We're writing this to deflect negative publicity." What my paper says is: Their collective responses within documents seem to focus on deflecting negative publicity.

Q. Again, that's your interpretation of this document, correct?

A. Yes, because the document discusses various mechanisms to dilute the findings by Dr. Pomeranz and others.

Q. Show me where it uses the word "dilute."

A. Well, "dilute" is my word.

Q. Is it reasonable for the company to attempt to understand the mechanism of NAION when faced with these reports?

A. To understand the mechanism?

Q. Yes.

A. Of course.

Q. And is it reasonable for the company to understand the context in which the cases of ION have been reported?

A. They are required to do that.

Q. And part of that is understanding the biological mechanism of NAION, correct, of how NAION occurs, or trying to understand how NAION occurs?

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A. Well, it's always interesting to know the pharmacology, but the mechanism -- we aren't required to know the mechanism of how a drug produces its beneficial effects, and we aren't required to know the mechanism by which it -- by which it triggers its negative effects. It's interesting to know it, but it isn't required for us to know it. I mean, many inserts will say after the indication, "We have -- we don't know how the drug causes this effect."

Q. So is it -- are you saying that the company was wrong in trying to understand how the drug would cause -- could cause NAION?

A. Oh, I think that all information is important. And I -- and I didn't say they were wrong to attempt to do studies to try to tease out, if that's what they were doing, the biochemical or pharmacologic mechanism. It's not required for them to do that for them to conduct the proper pharmacovigilance responses. And one doesn't --

Q. If the -- if the --

A. Let me finish.

And one doesn't delay follow-up pharmacovigilance activities while doing or planning or thinking about doing mechanism of action studies.

Q. Well, isn't part of your pharmacovigilance activity understanding the mechanism by which a drug

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could cause an event?
A. I don't think so. It's interesting to know, but one doesn't delay follow-up activities to tease out a mechanism.
Q. Getting back to Exhibit 2, which is the Guidance for Industry for Good Pharmacovigilance Practices.
It's right here, Doctor.
If you look to page 6, if you look right above the numbered list, it says, "In assessing case reports, FDA recommends that sponsors look for features that may suggest a causal relationship between the use of a product and the adverse event, including." And number 4 says, "Consistency of the event with the established pharmacological, toxicological effects of the product.." Right? That's what the FDA recommends, correct?
A. For causal relationship. But the FDA regulations and the FDA opinions also say that including information in your labeling is not dependent upon establishing a causal relationship.
Q. But the FDA recommends that you do look to see whether there is a causal relationship, correct?
A. You can, but you don't delay or avoid including it in your labeling while you toy with those types of studies. The regulations state that. And FDA's stated

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opinions by people such as Dr. Woodcock, Dr. Buhl, all state that causality is not necessary. It's been -- you don't delay for causality.
Q. Okay. I'm not asking you about causality. I'm asking you about whether Pfizer was -- did anything wrong by trying to understand whether there was a plausible biological mechanism by which Viagra could cause NAION.
A. It's never wrong to want to do additional studies. What I'm saying is -- I didn't say Pfizer was wrong to do studies. I said Pfizer was wrong not to inform patients and their prescribers.
Q. Now, the end of that sentence we've been talking about on page 13 of your report, you say that the company didn't perform the necessary epidemiological study to determine the relatedness of this adverse event to the drug's use.
That's what you wrote, correct?
A. Yes.
Q. And there's other ways to determine relatedness other than doing an epidemiological study, correct?
A. Well, for this particular drug, one couldn't do a prospective study, so one would have to do an epidemiologic study.
Q. Well, there's other ways to determine

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relatedness besides an epidemiological study, isn't there?
A. Yes, but they already had evidence of rechallenge. So the three ways of doing it are prospectiveness, prospective studies, retrospective studies, or rechallenge information.
Q. And is looking at biological mechanism one of the ways to determine relatedness?
A. Well, yeah, you can look at that. But that isn't what I'm referring to there.
Q. Okay. But that's something that the company did, correct?
A. Right.. But I'm referring to updating the product labeling.
Q. Looking at Exhibit 12, is there anything in this document that's incorrect?
A. Well, I'm -- I believe their conclusion to the first three pages is that there is not sufficient evidence to suggest that Viagra is causally associated with NAION. And I don't think that's incorrect. I don't think it's relevant to what I'm talking about, but it's not incorrect.
Q. The FDA was aware of these case -- of these case reports of NAION, correct?
A. Well, they were aware of the ones that were

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included in the update reports, and they were aware of the ones in AERS.
Q. Are you aware of any report for NAION that the company did not send to FDA?
A. I don't know.
Q. Do you agree with me that the FDA has information regarding this class of drugs beyond what Pfizer has?
A. Well, they would have information -- if other manufacturers were submitting information to them, they would have that.
Q. So they have the information being submitted in support of Levitra, correct?
A. I would imagine, yes.
Q. And Pfizer didn't have access to that, correct?
A. I don't know. I don't know, but I wouldn't think so.
Q. And they -- and the FDA would have access to information regarding Cialis, correct?
A. I would think so.
Q. And Pfizer wouldn't have access to that information, correct?
A. Not that I know of.
(Exhibit No. 13 was marked for identification..)
BY MS. LESKIN:

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Q. Exhibit 13, which is a document entitled "Dear Field Force Managers and Representatives," Bates stamped 002184799 through 800. And you've seen that document before, correct?
A. Yes.
Q.. And you cite that at the bottom of the paragraph on page 13 that we've been talking about?
A. Yes.
Q. And this document is prepared after Dr. Pomeranz's case series of seven patients in 2005, correct?
A. I believe so.
Q. In fact it's referring to Dr. Pomeranz's case series of seven new cases?
A. Yeah. It appears when it was published. I -- I -- I don't know the date, if they knew about it earlier than the date it was published. And I don't know the date that he submitted it.
Q. Is there anything in this document that's false?
A. I don't know if there is anything false. We are not permitted to do what is in the middle there, the underline bold "there is no evidence it occurred more frequently." We are not allowed to make those type of statements anymore because -- or actually they were

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never appropriate -- because we are compare -- what they're comparing there is the NAION from the seven events, and attempting to compare that with the normal incidences rate. And repeatedly FDA has said that's an unfair comparison because those seven events do not represent -- we have no way of knowing what the true incidences of the events are.
Q. What are you basing your view that this underlined sentence that says, "There is no evidence showing that NAION occurred more frequently in men taking Viagra than men of similar age and health who did not take Viagra," what are you basing your statement on that that is based on the seven reports in Pomeranz?
A. Because they're talking about the seven events in Pomeranz.
Q. Are you aware of any evidence showing that NAION occurred more frequently in men taking Viagra than men of similar age who did not take Viagra?
A. We don't know either way because labeling -- because adverse events only report 1 to 10 percent. We have no idea what the true incidences rate is. So because of that, we cannot represent that there's no difference from the background incidences rate. I mean, FDA has stated that. There have been letters written. I mean, there's a publicly available letter to Roche,

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with Accutane, that they could not say statements such as this because they don't know the true incidences rate of the adverse event.
Q. Are you aware of what data exists to back up Pfizer's statement that it's underlined in here?
A. Well, at this point they're talking about the seven cases.
Q. Where does it say that, that that statement is referring to the seven cases?
A. The lead paragraph is: "There's a case of seven." What else -- what -- what else are they referring to?
Q. Well, that's what -- Where is the evidence that those -- that that statement is referring solely to the seven cases published by Dr. Pomeranz?
A. Well, that was my impression, since it leads with that. And this is designed to help field representatives to respond to the Pomeranz information.
Q. So that's your assumption that that's what that's referring to, correct?
A. Yes.
Q. Now, on bottom of page 13, you list several bullets coming from a Pfizer document, which you describe as "several reasons to overlook Viagra as a risk factor in the onset of NAION."

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A. I'm sorry. I have to amplify that.
They say in this third -- second paragraph, "While there is no new information on this subject, from what we knew in March, the media has taken up the story again with great intensity. In response, Pfizer has issued the following statement to the media."
So they are referring to the Egan and Pomeranz reports.
Q. So it's your testimony that that statement you just read demonstrates that the underlying sentence means they're referring solely to the seven reports?
A. Well, they only refer to the seven reports and the clinical trial data. And since there were no reports in the clinical trial data, and the clinical trial used a population that is not indicative of the post-marketing adverse event information, that only leaves the Pomeranz reports that they're referring to here.
Q. Looking at page 13 of your report again, at the bottom there's a list several bullet points comes out of a document, which you said are several reasons that Pfizer noted to overlook Viagra as a risk factor in the onset of NAION. Do you see where I am?
A. Yes.
Q. Okay. In that first bullet you wrote, "No

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reason to believe that Viagra decreases blood flow to the vessels supplying the optic nerve head."
Is that a true statement?
A. Do you have the document?
Q. I'm on page 13 of your report.
A. No, I mean the document to which it's referring.
Q. Well, I'm just looking at the sentence you quoted. Do you have anything to say that that statement is not true?
A. I'm just trying to see the document because I have it in quotes.
Q. Okay. It's Exhibit 12. That's what you cite, I should say.
MR. BECNEL: Ms. Leskin, on Exhibit 13, do these two documents go together? The page 1 and page 2 are 799 and 800.
MS. LESKIN: They follow in Bates stamp.
MR. BECNEL: Yeah. But if you look at the front page where they send Dear Field Force Managers and Representatives, they say "23 million men have used it worldwide." Then on the next page, which is supposed to be attachment, they say "26 million men have used Viagra since its introduction." Which is true? Are they not the same document?

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MS. LESKIN: They follow each other in Bates number.
MR. BECNEL: I didn't ask that question. I asked you if you got 3 million -- you got 3 million people --
JUDGE BORG: I think the answer is: "I don't know."
MR. BECNEL: Okay. She --
MS. LESKIN: The answer is: I'm not obligated to respond to your question --
MR. BECNEL: You are if it's a false document.
MS. LESKIN: It's a document she cited.
MR. BECNEL: It's not -- no. You produced this. We didn't have this.
MS. LESKIN: She cited it in her report.
MR. BECNEL: Yes.
MS. LESKIN: That's why I'm asking about it. That's it.
MR. BECNEL: Because it's a confidential, subject to protective order. We didn't produce that.
MS. LESKIN: Mr. Becnel, if you wanted -- had a question about the substance of the document, you could have taken discovery of our witnesses. You chose not to ask anyone about the document.

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JUDGE BORG: Ms. Leskin, please continue with Dr. Blume.
MS. LESKIN: Thank you.
MR. BECNEL: I'll just point out to the jury the falsity of how Pfizer does documents.
JUDGE BORG: Okay. So let's get going with the deposition.
THE WITNESS: Okay. I'm looking. I'm trying to track it. I see --
JUDGE BORG: Do you remember the question?
THE WITNESS: Yes.
BY MS. LESKIN:
Q. We're talking about the first bullet at the bottom of page 13.
A. Yes. And I started -- I'm tracking the quote marks to this document.
Let's see. A delay of two days following is Point No. 3 on page ending --
Q. I want --
A. -- 08.
Q. I want to focus on bottom of page 13, your first bullet. You quoted the statement of "several reasons to overlook Viagra as a risk factor in the onset of NAION." And you wrote, quote, "No reason to believe that Viagra decreases blood flow to the vessels

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supplying the optic nerve head."
My only question is: Do you have any evidence that that is a false statement?
A. I put it in quotes, and it's at -- it's on your page 08. I took it right from this document. "No reason to believe that Viagra decreases." I took it directly from your document.
Q. Okay. Do you have any evidence that that is a false statement?
A. I'm a little confused. I didn't say they were false statements. I said they collected these statements in an effort to deflect the information relating to NAION. And then I quoted them directly from your client's documents. But nowhere in there do I -- have I misquoted them, that I've seen so far, and nowhere did I say they were false.
Q. Okay.
A. I said they included these as alternative reasons to the NAION.
Q. Doctor, my question is: Is that a false statement?
A. Not that I know of, based on the information I have, nor did I say it was false. I said they used it to avoid the true issue.
MS. LESKIN: Move to strike. Objection;

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nonresponsive.
JUDGE BORG: It's overruled.
BY MS. LESKIN:
Q. The next bullet point: "Several Pomeranz case reports," quote, "have aspects to their descriptions which must be considered suspect when suggesting a causal association between the development of NAION and the use of Viagra," end quote.
Do you have any evidence that that is a false statement?
A. Oh, I -- I don't know if anything suspect in the Pomeranz case reports. I'm not sure to what they're referring.
Q. Do you disagree with that statement, then?
A. I don't have enough information either way. But I'm using -- the quotes are because it comes from your report. And moreover, it's in there to deflect, in my opinion, to deflect concerns from the Pomeranz data by calling upon the doesn't support a causal association. It doesn't matter if it suspects a -- is a causal association. The clinical data showed that it occurred.
Q. Are you saying that the company shouldn't have tried to understand whether there was a causal association, it didn't matter whether there was a causal

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association to the company?
A. It may have mattered to the company. The problem is, it shouldn't matter to the extent they didn't put it in their labeling, and it's inappropriate to fall back on inadequate data to -- to support causation in an effort to dilute the importance of the events.
Q. Is it inappropriate to try to disseminate truthful information?
A. What? No, it's not inappropriate to submit truthful information. It's inappropriate to hide truthful information.
Q. Do you have any evidence that Pfizer tried to hide information?
A. Well, they didn't put it in their labeling.
Q. The third bullet point is: "Significant risk factors for vascular disease and/or NAION were described for several patients, including diabetes, coronary artery disease, hypercholesterolemia, smoking, and a previous episode of AION in the opposite eye with recent visual difficulties before starting to take Viagra," end quote.
Is that a false statement?
A. No. I think I quoted it directly from -- as you had it in your report, the client had it in their

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report.
Q. And do you have any evidence that that's not a true statement?
A. I'm not quite certain where you get that they're not true statements. I'm assuming that they're true. I quoted them directly assuming they were true. My point has nothing to do with their veracity.
Q. My question has to do with the veracity. Do you have any evidence that those statements are not true?
A. No.
Q. The next bullet: "Patients' age (52, 69, 42, 62, 59) and male gender provide two well-known risk factors for the development of vascular disease regardless of whether or not they had additional cardiovascular risk factors."
Do you have any evidence that that is a false statement?
A. I hope not, since I quoted it directly.
Q. The next bullet: "Two of these cases, the patients were on Viagra for long periods of time (15 months in one case, two years in another) with no prior episodes of AION."
Do you have any evidence that that is not a true statement?

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A. Yeah, I don't know either way. I assumed it was true because I quoted it directly, but I don't have the source documents to know that for sure..
Q. The last bullet says: "A delay of two days following the suspect dose of Viagra before a visual field loss was reported, although eye pain occurred the day following Viagra use."
Do you have any information that that is a false statement?
A. I don't know. I assumed it was true because I quoted it, but I have no idea because I don't have the source documents.
Q. At the end of the bullets, you wrote the sentence: "Unfortunately, the campaign to minimize a serious adverse event was successful."
Did I read that sentence correctly?
A. Yes.
Q. Is that an opinion you hold to a reasonable degree of scientific certainty?
A. Yes.
Q. What science are you using to reach that opinion?
A. Well, I quote a document where they are pleased that the story is over regarding the NAION.. And there is later in here a document that shows that the sales

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were maintained during that period. So if they're pleased that the bad news is over and the sales are maintained in the face of a blinding -- blinding -- permanent blinding in patients taking a recreational drug, then that is the basis for my statement.
Q. What science did you use to reach that conclusion?
A. Well, you keep asking that question. But these are personal opinions based on 30 years of experience. I can't point to anatomy or physiology. This is regulatory affairs.
Q. And that's your personal opinion?
A. Based on regulatory affairs, pharmacovigilance, the documents from your client, and 30 years in the business, yes.
Q. What aspect of regulatory affairs science goes to decide whether a campaign is necessary -- is -- a campaign designed to minimize serious adverse event was or was not successful?
A. What component of regulatory affairs?
Q. Yes.
A. Because I think they got one warning letter -- let me make sure of this.
I think they received a warning letter, but they did not have to withdraw the ad campaign.

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Yes. During that period, there was not any request by FDA to withdraw the ads, although -- yeah, they received two DDMAC letters, but there was no request to withdraw them.
Q. And it's your opinion that those two requests to -- that those two DDMAC letters constitute -- let me start again.
Is it your opinion that those two DDMAC letters were in response to a campaign to minimize a serious adverse event?
A. Well, the February 2001 says, "Contains written and graphic representations about Viagra, fails to include information relating to Viagra's major side effects and contraindications." So I think that one does.
And the next one says, "Your TV ads failed to disclose the drug's indication, fails to include information relating to its major side effects and contraindications."
Q. Does anywhere in the DDMAC letter say that Pfizer was required to include reference to NAION in its advertisements?
A. Well, no. But that isn't the question you asked me. The question is, did any of the --
Q. It's a new question. Is there anywhere in the

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DDMAC letters that says Pfizer was required to include reference to NAION in its advertisements?
A. The April 2008 letter is a warning letter, and it says that "The ads to patients, direct to consumer, fails to disclose risk information. The video raises public health and safety concerns through its omission of risk information by suggesting Viagra is safer than has been demonstrated."
Now, I don't have the specifics here for what went into that warning letter, so whether the absence of NAION was on that ad or not, I don't know. But that would have been after NAION was in the labeling.
Q. Okay. But that's not the campaign you're referring to on page 14, is it?
A. 14. Okay. I'm sorry. I'm lost. I was referring to your question regarding warning letter in 2008.
Q. Okay. This started as a discussion of the campaign to minimize a serious adverse effect, as referred to on page 13, in 2005 following the publication of Dr. Pomeranz's seven-case series.
Now, the letter date -- from DDMAC, dated April 16th, 2008, that's not part of the campaign you were referring to in 2005, is it?
A. No, of course not. Because I'm referring to --

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I'm referring to campaign in 2005 here. The warning letter in 2008 is a different issue. But I was responding to your question regarding warning letters.
Q. Okay. Is the February 2000 DDMAC letter part of the campaign that you're referring to on page 14?
A. 14 is referring to the early days in 2005, after the Egan and Pomeranz data. The warning letter regarding failure to include safety information was in 2008.
Q. So I'm going to go back to my question, which is where we started the discussion of the ads.
I asked you: What aspect of regulatory affairs leads you to conclude that Pfizer ran a campaign to minimize a serious adverse event or that that campaign was successful?
MR. BECNEL: Objection; compound.
THE WITNESS: Okay. Oh.
JUDGE BORG: Are you able to answer that question?
THE WITNESS: No.
JUDGE BORG: Okay.
BY MS. LESKIN:
Q. Okay. I'll separate it.
I asked you earlier, what science supported your sentence on page 14 that the campaign to minimize a

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serious adverse event was successful. And you told me that that sentence was your personal opinion based on 30 years of regulatory affairs experience, correct?
A. No. I think I said more than that, but that was included in what I said.
Q. Okay. So my question is: What aspect of regulatory affairs leads you to reach the opinion on that first sentence under the bullets on page 14?
A. Well, regulatory affairs is the science design that includes providing labeling and marketing and advertising information and being consistent and maintaining consistency with FDA regulations.
My answer was, that while they received two DDMAC letters and one warning letter regarding Viagra and not providing all necessary safety information, they were not associated with these events, with this -- with this information I'm proposing -- or he's summarizing in page 14.. So from that prospective they did not receive a warning letter or a DDMAC letter on this.
My other answer to that was: They were pleased with themselves, congratulating themselves that their approach was able to trigger the continued sales of Viagra notwithstanding this adverse information, and that they maintained their sales. They say, "Our business goal was to maintain the number-one position in

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the ED market." And they were pleased because they think that they resumed it because they were able to capture relapsing patients.
So those facts underlie my feeling that their campaign was successful.
Q. You don't have the opinion that Viagra should not be on the market today, do you?
A. I know you asked me that before. And I think I said no. I am not saying that it's -- should be withdrawn.
Q. Okay.
A. What I'm saying in this report is, it didn't have adequate labeling.
Q. Okay. And if a drug is legitimately and legally on the market, is there anything wrong with the company wanting to sell the drug?
A. I think that a company should want to sell their product if they believe in their product. Of course they should. But I think inherent in that obligation, inherent with their obligation and reward of selling a drug and having a billion-dollar-per-year drug is that they provide prescribers and their patients with all available safety information. And that is especially important for a drug such as Viagra that is unnecessary.

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So with the -- with the joy of making it -- having multibillion-dollar-per-year drugs is the obligation that you maintain adequate labeling. And that is my issue with Pfizer and the Viagra labeling.
Q. So the fact that the company wanted to continue selling Viagra and maintain the number-one position in the ED market for sales, you don't necessarily find fault with that, do you?
A. Of wanting to have a number-one product? No. I find fault with not -- with having a number-one product while not providing important safety information, especially for a lifestyle drug.
Q. What document says, "We want to have the number-one product, but we don't want to provide the right safety information"?
A. I didn't say there was a document. I said that they did want to provide it, and they didn't amplify their labeling. So they did say they wanted the number-one drug, and they didn't amplify their labeling until they were forced to by the FDA.
Q. Is there anything wrong with wanting physicians to understand changes to your label, the company wanting to -- for physicians to understand changes they make to the label?
A. No, of course not. That's why when changes are

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made to labeling, Dear Doctor letters are sent, a variety of things can happen. But the labeling has to be changed first.
Q. So on page 14, that bottom part of page 14, where you say "By 2006..." Do you see that?
A. I'm sorry. Just one second.
Q. Sure.
A. Yes.
Q. Now, by 2006, the Viagra label had been changed, correct?
A.. Yes.
Q. That happened in July 2005, correct?
A. Yes.
Q. So where Pfizer said that their business goal was to maintain the number-one position in the ED market, that was after they changed their label, correct?
A. Yes.
Q. And their plan to support physician understanding of label changes, that also was after they had changed their label, correct?
A. Yes. That they were going to -- they were going to do that by attempting to re-attract lapsing Viagra patients, increasing information with regard to alpha blockers and ION as they arise.

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Q. Is there anything wrong with that?
A. Well, the labeling had been changed. I would hope they would be trying to support physician understanding of NAION.
Q. So there's nothing wrong with that, then, is there?
A. Helping physicians understand?
Q. Correct.
A. No. I would hope they would help physicians understand.
Q. Or reducing the lapse in Viagra patients. Do you have a problem with that?
A. Focus on reducing lapsing of Viagra patients. I'd have to go back and check that document. I can't remember that document specifically.
Q. Bottom of page 15, you refer to the McGwin study?
A. Yes.
Q. Do you agree with me that the McGwin study did not find an increased rate of NAION in patients overall, taking Viagra -- strike that. That's a bad question.
Do you agree with me that the McGwin study did not find an increased rate of NAION take -- in patients taking Viagra overall?
A. Yes.

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Q. You also wrote here that, "A statistically significant association was observed in those patients with a history of myocardial infarction."
Do you see that?
A. I do.
Q. And that's based on the published article, correct?
A. Yeah, I'm referring to the publication here.
Q. Okay. Did you read Dr. McGwin's deposition in this case?
A. Yes.
Q. Both of them?
A. Oh, I don't recall if there were two. I don't know.
Q. Do you recall reading a deposition that was taken on December 11th?
A. I think that was the one where they discuss two patients in the study, errors with two patients?
Q. The one where they discussed errors in the study.
A. Yeah, I do recall that.
Q. Okay. Do you recall Dr. McGwin's testimony that he had assumed that the information he was provided dealt with a personal history of myocardial infarction in those patients? Do you remember reading that in the

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deposition?
A. I remember discussing -- I remember reading that he was discussing a couple of errors. I do remember that. I don't remember the specifics, though.
Q. I want you to assume with me, hypothetically, that the authors of the McGwin study did not investigate the subject's prior history of myocardial infarction. Would that make the reporting findings about the association in patients with a history of myocardial infarction, as you cite in your report, unreliable?
A. Oh, I don't know. I'd have to know the whole story. But it doesn't impact my -- none of these studies really impact my opinion because I don't believe that the reporting of blindness in ION and NAION is dependent on what's going on in the other studies. And the McGwin study only has, I think, 30 or 40 people in it anyways.
Q. Did the McGwin study study blindness?
A. I thought it -- I thought they used the term, the specific term NAION, but I'd have to look at the study again.
Q. Do you have an opinion here today whether Viagra causes blindness as you've used the term?
A. I didn't use the term "cause." I used the term that blindness has been reported with Viagra. And it

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was the inclusion of permanent blindness was delayed in the labeling. There is -- it's very difficult to separate out blindness, optic neuritis, ION, and NAION because of the way the coding of these events occur. So I have tried very hard to look at the events of interest, which are the ones that might lead to blinding. I mean, the way these are coded, it might be optic neuritis, it might be ION, it might be NAION, it might be blinding. So I have tried to look at the ones of most concern to me, and those are the ones with blinding.
MS. LESKIN: Objection; nonresponsive.
JUDGE BORG: I'll overrule.
BY MS. LESKIN:
Q. Let me ask the question again.
Do you have an opinion here today whether Viagra causes blindness as you have used the term blindness?
MR. BECNEL: Objection; asked and answered.
THE WITNESS: I have not been answered -- asked to look at causation.
BY MS. LESKIN:
Q. And you're not going to be giving an opinion in this case regarding causation of blindness; is that correct?

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MR. BECNEL: Let me enter an objection. That's repetitious. You covered that the first 15 minutes of this deposition, Counsel.
MS. LESKIN: Well, no, I didn't.
MR. BECNEL: Why are we going back over it a second time and third time?
MS. LESKIN: I specifically asked about NAION.
JUDGE BORG: You know what? Counsel is not going to argue with each other. It's overruled. Would you please restate the question.
BY MS. LESKIN:
Q. I just want to be clear that you are not offering an opinion in this case regarding causation of blindness.
A. It is my understanding I will not be.
Q. Now, you wrote on your report here at the end of page 15, top of 16, regarding the McGwin study, that: "Given the results observed and the potential significance of the associated adverse events, these results should not be diluted or ignored."
Is it your opinion that Pfizer ignored the McGwin study?
A. I don't know. I don't know.
Q. Is it your opinion that Pfizer diluted the McGwin study?

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A. I think that most of the Pfizer reports have focused on background incidences and the pulling of data by the Gorkin -- in the Gorkin paper, and have criticized the other studies. And my opinion, as I've addressed all day, is that it's inappropriate to dilute the significance of the adverse event finding by incidences studies.
And I think that the Pfizer experts have largely have criticized the Margo and French study and the McGwin study, and focused on the -- on the Gorkin study as an effort to address the importance of the NAION events relative to population indices. And I disagree with that approach completely.
So in that respect, I think that they have ignored what is important by those efforts. But other than that, I don't think I have made any other -- have any other comments regarding their efforts with the -- with the McGwin study.
Q. When you referred to the Pfizer experts, are you talking about the experts in this litigation?
A. Yes. I recall reading their reports, and they dismiss the importance of many of -- of the NAION events in an effort to compare them to background incidences. And I recall in those reports, they also talk about some of the frailties with the various studies. And I recall

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the McGwin study is included in some of those. But I disagree with that approach. I don't think that you can estimate -- put any perspective on the relevance of an important adverse event by comparing it to a background incidence when we know that only 1 percent of the adverse events are known to us.
Q. Okay. That's -- that -- again, to be clear, you're referring to statements made in the context of this litigation, correct?
A. Yeah. I think I'm referring to the reports that were provided to me.
Q. In this litigation?
A. Yes. But I --
Q.. But you're not --
A. I don't believe that I ever said that -- I don't believe I ever said that Pfizer in public diluted -- I would have no reason to say in public diluted the significance of the McGwin findings..
Q. That was my question. Thank you.
I want to turn to the bottom of page 16 of your report.
A. Yes.
Q. You have a series of reports -- of literature here at the bottom of page 16 where it says, "Additional adverse ophthalmologic events in association with

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sildenafil have also been published in the medical literature soon after the launch of the product."
Do you see that at the bottom?
A. Yes.
Q. And then you cite a whole bunch of reports?
A. Yes.
Q. What event was at issue in the Donahue report?
A. Which ophthalmic event? I don't -- I don't recall specifically. But I have everything here if you want me to get it.
Q. Oh, I have them.
A. Okay.
Q. I just was seeing if there was a way to shortcut it.
A. Uh-uh.
Q. 14 we're going to mark as the Donahue case support entitled "Pupil-Sparing Third Nerve Palsy Associated With Sildenafil Citrate (Viagra)."
(Exhibit No. 14 was marked for identification.)
BY MS. LESKIN:
Q. And that's the Donahue article you cite at the bottom of page 16 of your report?
A. I believe so.
Q. Okay. And you'll agree with me that this refers to third nerve palsy, right?

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A. Yeah. I think the reason -- well, first of all, this paragraph is all ophthalmologic events. And of interest in this one is that the editor -- or the writer notes that it suggests that system -- systemic hypotension sufficient to cause dysfunction can be induced by sildenafil without other products. And I think I was interested in that because it's a -- it's another hypotension, which is a similar mechanism of action as to what we fear may be involved with ION and NAION.

MS. LESKIN: Objection; nonresponsive.

JUDGE BORG: Sustained.

BY MS. LESKIN:

Q. This article deals with --

JUDGE BORG: Five minutes.

BY MS. LESKIN:

Q. This articles deal with third nerve palsy; correct?

A. Yes.

Q. Is it your opinion in this case that Pfizer should have amended its label to include third nerve palsy?

A. No, nor do I say that. This is simply an overview of other ophthalmologic events.

For example, the reason Tripalzi and O'Donnell

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are in there in 2000, is they have a plea in their article that this information regarding the -- the retinal event should be made public so that physicians can describe it and share it with their patients. And I -- that's why that article is in there. So as early as 2000, independent people were saying, "We need this in the labeling so we can share this with our patients."

MS. LESKIN: Objection; nonresponsive.

JUDGE BORG: Sustained.

BY MS. LESKIN:

Q. Is it your opinion in this case that Pfizer should have amended its label to include third nerve palsy?

A. Gee, I thought I answered that. But the answer was no. This is a combination of ophthalmic literature. We can go through them one by one. The reason this one is in here, it's a similar mechanism of action. And you'll note that they do use the word "cause" in this one.

MS. LESKIN: I'll object to everything after the word "no."

JUDGE BORG: As nonresponsive?

MS. LESKIN: As nonresponsive.

JUDGE BORG: Sustained.

BY MS. LESKIN:

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Q. Are you familiar with the Vobig article?

A. Oh, I don't specifically recall it. We can look at it.

(Exhibit No. 15 was marked for identification.)

Q. Exhibit 15 is Vobig, "Retinal Side Effects of Sildenafil."

This article deals with retinal side effects, correct?

A. Yes. And what's important in this article is that the authors, as early as 1999, were agreeing that the long-term effects should be clarified by further studies. So that's why I included this article.

MS. LESKIN: Objection as nonresponsive everything after the word "yes."

JUDGE BORG: Sustained.

BY MS. LESKIN:

Q. Dr. Vobig attributes the retinal effects on the inhibitory effect on phosphodiesterase 6, correct, if you look at the bottom of his -- of his article?

A. That's what he thinks.

Q. And he's -- and he is advocating further studies on the long-term effects of sildenafil on retinal function, correct?

A. Correct.

JUDGE BORG: Want to find a break here?

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MS. LESKIN: Yep. One more question, then I will.

JUDGE BORG: Sure.

BY MS. LESKIN:

Q. You'll agree with me that there was information about the effects of PDE6 in the Viagra label from the time of its initial approval, correct?

A. Oh, I think so.

MS. LESKIN: We can take a break.

THE VIDEOGRAPHER: We're off the video record.

(Recess from 3:44 p.m. until 3:57 p.m.)

THE VIDEOGRAPHER: We are back on the video record.

(Exhibit No. 16 was marked for identification.)

BY MS. LESKIN:

Q. We have marked as Exhibit 16 an article that is by Dr. Burton, a letter to the journal. And that's the Burton article you referenced, correct, on page 16 of your report?

A. I think so.

Q. And the article is entitled -- or the letter is entitled "Sildenafil (Viagra), A Cause of Proliferative Diabetic Retinopathy," right?

A. That is the title, yeah.

Q. And we talked a little bit about diabetic

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retinopathy before. I just want to make sure that the publication of this case report doesn't support your opinion that -- well, strike that. Let me phrase that better.

I want to make clear that it's not your opinion that this article should have caused Pfizer to amend its label regarding NAION..

A. No. That isn't what any of those are in there for.

Q. Okay. And is it your opinion that the label should have been amended to include diabetic retinopathy, based on this case report?

A. You know, I don't know. I wasn't asked to study that, so I don't -- I don't have an opinion on that.

(Exhibit No. 17 was marked for identification.)

BY MS. LESKIN:

Q. Exhibit 17, this, I believe, is Murata. And there's some -- are you with me on 17, Doctor?

And even though it looks like most of this article is in Japanese --

MR. BECNEL: Are you going to read it?

MS. LESKIN: I am not going to read it.

MR. BECNEL: Are you going to read it and interpret it for us? I want --

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MS. LESKIN: Would you be impressed if I did?

JUDGE BORG: Yes.

MS. LESKIN: If you look at the last page, there's an abstract in English.

MR. BECNEL: I'm sure she went to school for three months to learn it.

MS. LESKIN: It actually says Viagra doesn't cause NAION.

BY MS. LESKIN:

Q. Do you see the abstract in English on the last page?

A. Yes.

Q. Okay. And this is regarding central serous chorioretinopathy, right?

A. Yes.

Q. And this article doesn't support your view that Viagra's label should have been amended to include NAION, correct?

MR. ALTMAN: Objection; foundation. She just said "this article." It's in Japanese. We don't know what it says.

MS. LESKIN: Well, let me -- I'll rephrase the question. It's -- I'll rephrase.

JUDGE BORG: She's referred -- well, I don't have --

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MR. ALTMAN: She said "the article" -- she said "the article," not "the abstract," is my only concern.

MS. LESKIN: I'll rephrase the question.

JUDGE BORG: Okay.

BY MS. LESKIN:

Q. You're not using this abstract to support your view that the Viagra label should have been amended to include NAION, correct?

A. No. This paragraph says that there were many ophthalmologic -- there were many reports relating to ophthalmologic events in the period following the launch --

Q. And this is --

A. -- of Viagra.

Q. -- just one of those, correct?

A. And I tried to pick -- this one happens to be the year 2000. I tried to pick different events, different ophthalmic events. This one happens to say that, you know, it was in -- the cause -- it was the -- the problem was induced by sildenafil. But all of these relate to hypotensive events and common mechanism of action, and I thought it was important because there is so much -- so much overlap with the various vision events -- blindness, NAION, ION -- that I thought it was

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important to cover all three of those earlier in the report, and then look at other ophthalmologic reports that have been reported.

Q. Where does this say this was a hypotensive event, Doctor? And I'm referring to the Murata article.

A. Oh, I -- if I said that it was this one, most of them related to hypotensive events. I think this one said that it was -- let's see. Dilatation of the choroidal vein near the leakage site. So they talk about a dilatation of the choroidal vein, and that that led to congestion over the retinal pigment, epithelial tissue.

Q. Does that have anything to do with the mechanism by which NAION is caused?

A. We don't know. It could.

Q. Are you aware of any -- and I thought I asked you this before, but we'll talk about it again.

Are you aware of any study that shows that central serous chorioretinopathy is at all causally related to NAION?

A. No. I was speaking in a larger mechanistic way that it causes a -- can cause a hypotensive effect that may lead to a vasodilatation. And one of the theories is that that vasodilatation may lead to a congestive or a compartmentalization effect, which in the end leads to

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an anoxia of the ciliary arteries for the optic nerve.
Q. And are you relying on the Murata article or abstract for that?
A. No, not particularly.
Q. You're relying on the Donahue article for that?
A. Donahue?
Q. That was Exhibit 14, on third nerve palsy.
A. No. As I said, this says "adverse ophthalmologic events associated with sildenafil." I mean, there's many ophthalmologic events associated with Viagra, and this is a collection of them. And I think I told you that I put Donahue in there because they said it was causative.
Q. Okay. You also told me that you collected a bunch of adverse events because they were hypotensive and --
A. And some of them --
Q. -- of the same mechanism.
A. Some of them relate to hypotensive properties.
Q. So what I'm asking is: Are you have -- do you have any evidence or are you relying on Donahue as one of those articles?
A. Okay. That was number what?
Q. 14, third nerve palsy.
A. Well, it says that, "Although this is a single

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case, systemic hypotension sufficient to cause neurologic dysfunction can be induced by sildenafil without other drugs."
So they are -- they are also talking about -- yeah, they're also talking about hypotension.
Q. And is the mechanism by which third nerve palsy occurs related to the mechanism by which NAION occurs?
A. Well, this is a neurologic, but it -- in the beginning there is a hypotension which is believed to trigger the neurologic dysfunction associated with third nerve palsy. There is also hypotension associated -- believed to be associated with the events that lead to the damage that can be -- that is believed to be associated with NAION and ION. So the hypotensive properties are common, but what happens after that leads to different events. But there is a systemic hypotension that we have to be concerned with with both of those types of ophthalmic events.
Q. Are you relying on the Vobig article for the hypotensive events or the similar mechanism that you described for me?
A. Well, I've -- I've added them in here for a variety of reasons. And I think that many different authors from the beginning of the launch, 1998, until current talk about the concern with hypotension,

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vasodilatation, and various ophthalmic events. And while we're focused on blindness and ION and NAION, I think it's important to note that the drug does cause significant systemic hypotension and it can lead to several different types of ophthalmic events, and these are just a few examples.
MS. LESKIN: Objection; nonresponsive.
JUDGE BORG: Sustained.
BY MS. LESKIN:
Q. Talking about the Vobig article, Doctor, are you relying on this letter to support as one of the hypotensive or similar mechanism of action as NAION?
A. I'm not relying on it to be a similar event as NAION. I'm relying that multiple authors have been concerned with ophthalmic damage secondary to hypotension.
Q. Is Dr. Vobig concerned with ophthalmic injury secondary to hypotension?
A. Who -- which one are you on now? Vobig?
Q. The one numbered 15, Dr. Vobig.
A. Well, he's linking the change in retinal function simply with the pharmacokinetic data. I don't think he mentions -- I don't think he takes it to the next step and wonders if the pharmacokinetic level somehow influences hypotension.

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Q. Does Dr. Burton, Exhibit 16, express a concern about hypotension?
A. Well, he says sildenafil -- "On the other hand, sildenafil is a potent vasoactive drug and diabetes fundamentally a vascular disease. Is it purely coincidental that such a dramatic deterioration in the retina should occur a few months following commencement of sildenafil?"
So I think he's looking -- yeah, he also is looking at the effects of it. It is a vasoactive chemical.
Q. Does -- is Dr. Burton expressing a concern about the hypotensive effects of Viagra?
A. Well, I don't know if he's expressing a concern. He's reporting a patient that has -- a long-term diabetic patient that had this event after -- a few months after starting the drug. I don't think he has enough information to be expressing a conclusion on it yet.
Q. Does he address at all the hypotensive response of Viagra?
A. Well, he discusses its vasoactive properties. And as far as I know, its vasoactive properties are largely -- largely limited to the systemic vasodilatation.

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Q. Show me where in this article he uses the term "hypotensive."
A. No. He -- I told you, he uses "vasoactive."
Q. And it's your -- it's your belief that he meant to say hyper -- "hypotension"?
A. Oh, I have no idea what he meant. I'm just telling you that vaso -- this product is a hypotensive agent.
Q. You're also telling me that you're relying on these articles because they express a similar mechanism or a hypotensive effect. So I'm asking you: Which of these articles express a similar mechanism or hypotensive effect?
A. And I told you that I answered -- I added these because they are other expressions of ophthalmic damage associated with Viagra. And in many of these -- well, actually it does say vasodilatation. It says it in the first paragraph, "Inhibition of PDE5 results in increased level of GMP, the intracellular messenger which affects vasodilatation."
Q. Okay. Where does that say "hypotension"?
A. Well, vasodilatation leads to hypotension. You're word parsing. All of this is the same thing. They all are looking at different ophthalmic events secondary to Viagra. And my point is that in many of

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these there is a concern with vasoactivity, vasodilatation, and hypotension.
Q. Was Pfizer's effect on blood pressure disclosed in the initial label?
MR. ALTMAN: Objection; vague.
JUDGE BORG: What's -- I sustain.
MS. LESKIN: I'm sorry. Yeah, I'm going to rephrase it.
BY MS. LESKIN:
Q.. Was Viagra's effect on blood pressure disclosed in the initial label?
A. I believe so.
Q. Was Viagra's effect on vasodilation disclosed in the initial label?
A. Yes.
Q. On page 18 -- on page 18 you say, "Regarding the association between Viagra and NAION, and associated temporary or permanent loss of vision, several lines of evidence support the possibility of a drug-induced effect."
Right? Did I read that correctly?
A. The first -- you read the first sentence and the second sentence? I'm sorry.
Q. The second sentence of that paragraph on top of page 18.

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A. I think you read it correctly.
Q. Okay.
A. Wait.
Q. Now, you're referring to -- you refer first to Dr. Mahmud's article, correct?
A. Yes.
Q. Does Dr. Mahmud's article measure blood flow in the optic nerves, in the optic vessels?
A. Well, I'll have to see it. But I don't know. From what I understand, it's not possible to accurately measure it in the fine -- in the fine optic vessels.
Q. Talk about the animal studies. Second paragraph talks about the animal studies supporting the biologic plausibility of Viagra inducing NAION. Now, you reference Hotta as one of those articles that demonstrate that, correct?
A. Well, I used Hotta to suggest that there might be biphasic effects.
Q. Well, is that one of the articles that you used to support your statement that results from animal studies support the biologic plausibility of Viagra inducing NAION?
A. Yeah. And I specifically used Hotta because I believe that was the one who talked about biphasic effects.

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(Exhibit No. 18 was marked for identification.)
BY MS. LESKIN:
Q. Exhibit 18, an article by Dr. Hotta.
A. I'm sorry. Did we do Mahmud? I lost track here.
Q. No. I skipped over that one for now. I'm on to the animal studies.
MR. BECNEL: Can I get one, please?
MS. LESKIN: I don't think I have an extra copy. The only copies I have are half and gobbly-gook or miscopied. You guys will have to share.
BY MS. LESKIN:
Q. Sorry. Exhibit 18 is Dr. Hotta's article, correct?
A. 18. Yes.
Q. And that's the article that you refer to here on page 18, right?
A. I believe so.
Q. Okay. Is Dr. Hotta studying sildenafil?
A. I don't believe so. It's a cyclic AMP phosphodiesterase inhibitor. I think at this point it was experimental.
Q. Does Viagra have an effect on cyclic AMP?
A. I -- I don't believe so.

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Q. So does this article demonstrate the biological plausibility of sildenafil, even creating a biphasic effect on ocular blood flow?
A. Let me see. I don't think directly, but it was the article that I -- the reason it's in here is, there are different theories as to how it may -- how ION and NAION may occur as it -- as a result of hypotensive properties and how does the vasodilatation cause it. And they seem to conflict because one talks about increased blood flow in congestion, and the other talks about deprivation of blood flow. And this article talks about by biphase -- biphase -- that a biphasic property can be present in retinoid blood flow, and that's why it's in here. It's one of the few articles that talk about that it can be biphasic. So it may not need to be one or the other. It may be a biphasic effect.
Q. Do you have any evidence that sildenafil produces this biphasic effect?
A. No. It's simply addressing that there's -- that the reduced blood flow may cause a congestion or may cause a deprivation.
Q. Okay. Do you, Dr. Blume, sitting here today, have any evidence that sildenafil causes a biphasic effect on ocular blood flow?
A. No. But that's -- no. And that's not the

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purpose of why this is in here. The purpose of it in here is showing that it's possible in the retinal tissues to have both a gorging effect and a deprivation effect.
Q. Dr. Blume, you wrote in your report, "Results from animal studies also support the biologic plausibility of Viagra inducing NAION." The very first article you cite is the Hotta article for the proposition that a phosphodiesterase inhibitor produced biphasic effects on ocular blood flow.
A. Well --
Q. So I'm asking you today: Do you have any evidence that Viagra or sildenafil produces a biphasic effect on ocular blood flow?
A. No. And that's not why it's in here.
(Exhibit No. 19 was marked for identification.)
BY MS. LESKIN:
Q. Exhibit 19 is an article by Behn and Potter entitled "Sildenafil-Mediated Reduction in Retinal Function in Heterozygous Mice Lacking the Gamma Subunit of Phosphodiesterase." That's the next article you cite in that paragraph, correct?
A. Yes.
Q. And this is an article in a study of mice with retinitis pigmentosa, correct?

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A. Correct.
Q. And it studies the effect on PDE6, correct?
A. Correct.
Q. How does the effect on PDE6 support the biological plausibility of Viagra inducing NAION?
A. Because one of the theories relating to NAION is unrelated or perhaps additive to the vasodilatation properties in that there's a direct renal -- or retinal toxicity. And this -- this article is addressing a renal toxic -- direct renal toxic -- a renal -- direct renal toxicity with the drug.
Q. Renal or retinal?
A. If I said renal, I met retinal.
Q. Okay. What article supports the theory that Viagra is direct retinal toxicity causes NAION?
A. Okay. Well, no article ever says that one effect causes it. But among the article -- among the different discussions is vasodilatation with congestion, vasodilatation with oxygen starvation, and perhaps some direct retinal effect.
Q. Okay. What article discusses a direct retinal effect that causes NAION?
A. Okay. None of -- again I will correct you. None of the articles will say "cause NAION." They are potential pathways associated with retinal dysfunction

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that may lead to ION or NAION, but none of them will say "cause."
Q. Okay. What article supports --
A. Oh, I don't --
Q. -- the hypothesis that Viagra causes NAION through a direct retinal toxicity?
A. None of them use the word -- none of them -- none of them that I know will use the word "cause."
Q. I didn't ask you cause. I asked you hypothesize. What --
MR. BECNEL: Wait.
BY MS. LESKIN:
Q. -- article --
MR. BECNEL: Wait, wait. Objection.
JUDGE BORG: Well, let's -- let's hear the question.
MR. BECNEL: That's exactly what you said twice.
MS. LESKIN: Fine. I will -- I'll rephrase the question.
MR. BECNEL: Well, let's read the transcript.
MS. LESKIN: I'll rephrase the question.
JUDGE BORG: She can rephrase the question.
MR. BECNEL: I understand, but she -- she --
BY MS. LESKIN:

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Q. What article gives the hypothesis that Viagra may lead to NAION through direct retinal toxicity?
A. Gee, I don't know. One of the articles. And I think it's -- addresses various mechanisms by the experts.
Q. Which article, Doctor?
A. I don't -- I don't recall a specific article. I just recall that there's three plausible articles, and direct retinal toxicity is probably the least of the three. But this was an example of being able to cause a direct retinal toxicity.
Q. Does Dr. Behn and Dr. Potter say that Viagra causes a direct retinal toxicity?
A. I don't know.
Q. Does Dr. Behn and Dr. Potter say that Viagra may cause NAION because of its effect on PDE6?
A.. I don't -- oh, I don't know. I doubt it. It's a mouse model. And you know from your work -- your client's work that the mouse model doesn't reflect humans. But it's -- it's -- all of these articles address which you have said many times today, that it's appropriate to go out and gather as much information you can in various models to attempt to describe what action the drug may be having. And that's what these do. They look at different aspects of the known actions -- they

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look at different aspects of the actions of sildenafil, and hope to try to address what actions might be leading to ION and NAION.
Q. You say in your report, Doctor, that this article supports the biologic plausibility of Viagra inducing NAION. Where is that support in this article?
A. That is what I believe. I believe there's three different ways that it may happen, and that this article was one of the few that I have seen that looks at direct retinal toxicity.
Q. What's the basis for that belief?
A. Just my accumulated reading. And really, none of this is material to my report about labeling because labeling is independent of biologic mechanisms.
Q.. So you are not going to give -- on the stand in front of a jury, you're not going to make the statement that the animal study supported the biologic plausibility of Viagra inducing NAION?
A. I think what I would say is that the clinical data have shown that Viagra caused or is associated with blindness, ION, and NAION, and it was known from 2000, and that we know from various animal models that Viagra influences phosphodiesterase 5 and phosphodiesterase 6, and those actions may both have impact on ophthalmic function.

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Q. Okay.
A. And that's as -- probably as much as I will say about biologic plausibility.
Q. When you say "ophthalmic function," you don't mean to say that PDE6 has an effect on NAION, correct?
A. No. I've said many times today that the PDE6 is believed to be due to the blue and green tinges, one other ophthalmic dysfunction.
Q. And so you're not going to offer the opinion that the Behn and Potter article provides evidence that supports the biologic plausibility of Viagra inducing NAION; is that correct?
A. I think I will say that there are collections of articles in different animal models showing that Viagra has various influences on retinal function. And I may show that this is a direct -- believed to show a toxicity on retinal function.
I don't know what I'll say because it will depend on what question I am asked.
Q. There's a difference, Doctor, between retinal function and NAION, correct?
A. Yes. But I'm talking about biologic plausibility.
Q. And I am, too. But I'm asking you: Is there a difference between retinal function and NAION?

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A. Yes, of course.
Q. And so when you wrote the statement in your report, "Results from animal studies also support the biologic plausibility of Viagra inducing NAION," I'm trying to figure out which studies you're referring to. And so far we've talked about Hotta, which doesn't address sildenafil, and we talked about Behn and Potter, which you told me originally supported a direct retinal toxicity.
A. Well, what the authors say is, these data -- these data and other model systems could be useful in understanding the mechanisms of RP and other forms of retinal degeneration. And sildenafil is associated with end -- end events that may well be the function of retinal degeneration or retinal apoptosis. So that's why this is instructive.
Q. Is NAION retinal degeneration?
A. No. But there is a inability to process the signals with NAION. And no one knows the complete evolution of the events that lead between hypotension and blindness, and what that cascade of events is. And if we have information that sildenafil is a direct retinal -- has a direct retinal impact, and this author thinks it may be important in other forms of retinal degeneration, then I would say it's important to look at

this.
Q. And Viagra -- Pfizer included on the Viagra label, from the beginning, the effect on PDE6, correct?
A. Yes, the FDA label noted that it does have an effect on PDE6..
Q. And it's well known in the --
A. It isn't PDE6 --
Q. It's well known in the medical community that PDE6 is in the retina, correct?
A. Oh, I – I know it. I have no idea if it's well known across the medical community. I'm sure ophthalmologists know it.
(Exhibit No. 20 was marked for identification.)
BY MS. LESKIN:
Q. I'm giving you Exhibit 20. It's an article by Dr. Vatansever and others. This is the next article cited in that paragraph, correct?
A. Yes.
Q. How does this article by Dr. Vatansever support the biological plausibility of Viagra inducing NAION?
A. It's another article that looks at histopathology associated with sildenafil and ophthalmic events.
Q. And how does this article support your statement about the biological plausibility of Viagra

inducing NAION?
A. Oh, I take it back. He does say, "Sildenafil is potentially retinotoxic due to the increase in retinal CGMP, suggesting clinical toxicity of the retina." So I guess there is one more -- there is -- he does -- he is noting several people who have looked at direct retinal toxicity. So I may have to amplify my earlier statement that it appears to --
Q. Well, I'll ask you --
A. -- be the least -- the least considered.
Q. I'll ask you again: Is retinal toxicity associated with NAION?
A. That -- yeah, I think that's one of the theories, that maybe it is.
Q. I'll ask you again: Who has said that? Where is --
A. Well, we found --
Q. -- the support for that statement?
A. I don't recall -- I don't recall the exact publication.
Q. Do you have a basis for that statement, Doctor?
A. Yeah. That's my understanding, is that there's three statements. And I know the experts have denounced retinal toxicity in their reports, saying that there is little support for that, but I know it is one of the

ones that was considered. But it has no relevance at all to my opinion. But if it's important, I will go back and tell you which expert looked at retinal toxicity. But I can tell you that this doctor is looking at it as well, and has decided that perhaps it is retinotoxic. Not that any of this has anything to do with my opinion or my report but --
Q. Well, Doctor, if you're going to not -- if you're going to confirm that you're not going to get on the stand and read and make the statement that animal studies support the biologic plausibility of Viagra inducing NAION, that's one thing. But if you are going to say that statement to the jury, I'm entitled to know the basis for that opinion.
A. And I gave a series of animal articles that show that Viagra has -- has -- has had impact in various models in various -- in various animal models dealing with the retina.
Q. And I wanted you to show me the study that shows that direct retinal toxicity causes NAION.
A. Yeah, I just don't remember which article that I read that.
Q. Well, you'll be able to find that for me if you wanted to?
A.. Oh, I think so, yeah.

MS. LESKIN: We'd ask for any support for the statement that direct retinal toxicity is associated with NAION that the doctor is relying on in providing her opinion in this case.
(Exhibit No. 21 was marked for identification.)
BY MS. LESKIN:
Q. Giving you Exhibit No. 21, which appears to be an article by LaVail and others regarding retinal degeneration in the mouse. This is the article you cite further on in Exhibit 18, correct -- on page 18, I'm sorry?
A. Well, this is looking at other inherited retinal disturbances that are associated with GMP elevations.
Q. Okay. Is this the article you cite on page 18 of your study?
A. I -- I think this is the one. There's several 1974 ones, but I think this is it.
Q. And again this article deals with retinal toxicity, correct, or retinal degeneration? Is that correct?
A. Secondary to photoreceptor cell degeneration, yes.
Q. Does this article have anything to do with sildenafil?

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A. I think, as I indicated, this looked at other inherited forms of retinal degeneration and their examination of cyclic GMP.
Q. Does this have anything to do with ischemic optic neuropathy?
A. Well, indirectly. One of the -- one of the pivotal tenets of pharmacologic research is, you look at common mechanisms of action and see if they lead to similar or related disturbances in the same target tissue. And this is an instance where someone is looking at elevated GMP levels, looking at other retinal disturbances.
Q. Ischemic optic neuropathy is not a retinal disturbance. Didn't you tell me that earlier?
A. It's secondary to inadequate blood supply.
Q. That's not a retinal disturbance, is it?
A. Well, indirectly.
Q. Is this article by Dr. LaVail looking at inadequate blood supply?
A. No. It's looking at inherited -- in animal -- no. The -- the role -- the importance of this article is the cyclic GMP elevations.
Q. Is there any evidence that increased cyclic GMP -- elevated cyclic GMP causes NAION?
A. No. But a tenet of pharmacologic research is,

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you don't have an animal model short of monkeys that look at NAION. And one of the ways that pharmacologic research is done is, in those instances you look at common mechanisms or common disturbances. And this is a collection of articles. And one of the things that I looked at was to other retinal disturbances, other ophthalmic issues, are they dependent upon toxicity secondary to increase of the cyclic GMP. This is an example of one. You cannot make the direct link that this animal model is the same as the issues that may or may not impact humans who are blinded or suffer ION or NAION. That isn't the way pharmacologic research goes.
Q. Tell me how the study by Dr. LaVail on cyclic GMP in mice retina supports the biological plausibility of Viagra inducing NAION.
A. Because what they're looking at is, there's diminution in retinal function secondary to cyclic GMP. And then we know that cyclic GMP as an issue is increased with Viagra. So it's a link that cyclic GMP is not conducive to maximal retinal health.
Q. And what does what that have to do with the health of the optic nerve?
A. Well, cyclic GMP is an issue with both PDE5 and PDE6. And we don't know. No one knows the direct cause of this. This is a distillation, a constellation of

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articles that look at different mechanisms. And you can't dilute the importance of what they're looking at simply because you can't make a link to -- directly to NAION. Your client hasn't been able to find a biologic mechanism for NAION. It's marketed the product since 1998.
Q. But you, Dr. Blume, can say that this article supports biological plausibility of Viagra --
A. Sure, because --
Q. -- inducing NAION?
A. -- associated GMP.
Of course. We look at GMP. I didn't say it caused it. I didn't say it was directly. It shows that GMP is a negative player to ophthalmic events, to ophthalmic health.
Q. All the ophthalmic events are the same to you?
A. Of course they're not. I -- I separate them completely in this report. And I don't know why you have to be so denigrating in your tone. This is an effort in pharmacologic research. This is the way it's done.
MR. BECNEL: Don't feel singled out.
THE WITNESS: It's -- if you're not a pharmacologist, you can't understand this.
(Exhibit No. 22 was marked for identification.)

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BY MS. LESKIN:
Q. Exhibit 22 is a letter by Drs. Farber and Lolley, L-o-l-l-e-y. This is the next article cited on that page 18, correct?
A. Yes. This is an article, along with the one that we just had -- 1974, let's see, that was 24 years before Viagra was launched. And at that point they knew that GMP may be a concern with retinal function. And this is another article a couple years later, in 1976, where they're looking at retinal function with CGMP. So you see the connection was anticipated for several decades before the product was launched.
Q. And how does this article support the biological plausibility of Viagra causing NAION?
A. Well, what it does is, it is again a link 20 years in -- 20 years earlier that GMP is a problem for retinal function. So retinal function is a concern, and it -- so it suggests that an inhibitor, such as Viagra, with both PDE5 and PDE6 may be a concern with events -- with retinal events.
Q. Do you know if Pfizer considered this article at the time it conducted its research on Viagra?
A. I think I quote that. I said Pfizer was aware of these.
Q. And did Pfizer consider the evidence that

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you're talking about when it was doing its studying of Viagra?
A. Well, I don't know if it specifically considered this as they planned their animal studies. I don't know.
Q. Well, let's take a look back at Exhibit 5, which was the visual summary from the NDA.
MR. BECNEL: What page on that one?
MS. LESKIN: Well, let her pull the exhibit out first, please.
THE WITNESS: I have it.
MS. LESKIN: Okay. On page 15 --
MR. BECNEL: Well, Counsel, you can be courteous and answer. You're looking at it. I asked you a simple question to be able to be on track with you.
MS. LESKIN: Page 15, Counsel.
MR. BECNEL: Okay. Fine.
BY MS. LESKIN:
Q. And if you look at the bottom -- are you on page 15, Doctor?
A. I am.
Q. And if you look at that bottom paragraph, you will see there's reference to the LaVail and Farber articles, correct?

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A. Yes.
Q. And then it goes on to the Ulshafer article, which you also cite, correct?
A. Yes.
Q. And they specifically assess that when looking at the data that they got from their studies; isn't that correct?
A. Yes.
Q. And this document was submitted to the FDA, correct?
A. That's what you told me, yes.
Q. Well, this is part of the NDA, correct?
A. That's what I understood you to say.
Q. And if it is in fact part of the NDA, then it was submitted to the FDA; is that correct?
A. I guess that would follow.
Q. I want to turn to page --
A. Well, in fact this is why they cited those, because they were talking about direct -- direct retinal toxicity.
Q. As a cause of NAION?
A. No, associated with the drug.
Q. And that's why they did additional testing in humans of the eyes, correct, of visual function?
A. Which additional testing was that in humans?

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Q. During the clinical studies that were done during the clinical development program.
A. Well, I thought you were referring to -- it was required that they needed to do clinical studies, yes.
Q. And Pfizer in fact did do the clinical studies of visual function during the clinical development program, correct?
A. Well, they would have to because it -- it impacts PDE6. So they would have been required to do it, of course.
Q. And they did that?
A. Well, yes, because they had to get approved. They had to do them to get approved. I thought you were referring to postapproval studies.
Q. Turn to page 19 of your report, please. Your first sentence there says, "The continued accumulation of serious adverse ophthalmologic events associated with Viagra use and found in the medical literature, foreign and United States spontaneous adverse event databases and Pfizer's internal adverse event database should have prompted Pfizer to undertake a more thorough analysis of NAION-related events associated with the drug."
Did I write that -- did I read that correctly?
A. I think so.
Q. What type of analysis do you suggest Pfizer

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should have done?
A. Well, I mean, every – every analysis that they eventually did was prompted by the FDA. FDA had to go to them and ask them to reanalyze their clinical data, then FDA had to go to them, tell them to reanalyze their pharmacovigilance post-marketing data, and then FDA had to tell them to continue to report all of their events, all of their ophthalmic events, as 15-day relating to NAION, and then FDA had to force them to do a post-approval trial, that took them multiple years to get started.
So my comment here is, is that there was plenty of information prior to FDA putting a gun to their head to do these things that should have prompted Pfizer to do this on their own. I mean, certainly they shouldn't have waited till 2008 to do a epidemiology study to look at blinding for a lifestyle drug. So that's -- it is those events to which I am referring. Every major event done, completed to address NAION was at the hand of the FDA.
Q. Is it your testimony that Pfizer did not review its clinical data until the FDA made a specific request to?
A. I'm saying that FDA requested the clinical data be reviewed, the post-marketing data be reviewed, and to

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do a complete -- to do a Phase IV study.
Q. Is it your testimony that Pfizer did not do a review of its clinical data until the FDA asked for it?
A. Well, I'm sure that they reviewed their data as it was generated for their NDA and as – as they reviewed it during their periodic reports.
Q. So is it your testimony that after the initial reports of NAION came in, that Pfizer did not review its clinical database?
A. Oh, I'm sure they did. They referred all the time that they had no events in their clinical database. So I would assume they were going back and looking at their database. But FDA asked them to go back and look for events more than NAION, and FDA gave them a complete list of what events they were to review.
Q. And did they find any additional NAION events when they did that review?
A. I don't -- I don't believe, in their clinical database, which made it all the more important that they do the pharmacovigilance Phase IV study once the NAION events became apparent in 2000.
Q. When you say you don't believe in their clinical database, you -- what do you mean by that?
A. Oh, I believe in their clinical database. I mean, FDA approved it as a condition for approval..

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Q. I'm sorry. Did you -- I asked you the question, did they find any additional events when they did that review, in the clinical database. And you said, "I don't believe in their clinical database."
A. Oh, I don't believe that they found any in their clinical database.
Q. Okay. And you just don't know whether they went back and had reviewed the clinical database before the FDA asked them to do that?
A. I don't recall that they reviewed it using the litany of terms that FDA forced them to use, no.
Q. And you said that they only went back and looked at their adverse event data when the FDA asked them to do that?
A.. No. I said FDA required them to do a comprehensive study of their post-marketing data, and then when that was conducted, they required them to continue submitting 15-day reports even for the listed events.
Q. So is it your testimony that before FDA made that request, that Pfizer did not do a comprehensive review of their post-marketing data?
A. They were required to review post-marketing data. You have to submit periodic safety update reports. It wasn't of the complexity and completeness

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that FDA required.
Q. And what's your basis for that statement?
A. FDA sent them a list of terms to use.. Pfizer went back with additional terms -- or negotiated other terms. And then Pfizer did their -- did the review and submitted it to FDA.
Q. And did they find any additional NAION cases?
A. I don't recall. I don't know.
Q. Is it your testimony that Pfizer did not submit 15-day reports for NAION before the FDA asked them to?
A. No, I didn't say that. I said that FDA told them they could not stop submitting them even though it was now a listed event, that they had to continue submitting 15-day reports.
Q. And that was after the label was changed, correct?
A. Oh, of course, because that's when it became a listed event.
Q. Now, let's talk about that label change in 2005.
As it currently exists, do you believe the current label is inadequate?
A. As it relates to what?
Q. As it relates to NAION.
A. No. I think the language for the NAION

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inclusion was negotiated with FDA, and FDA was part of that. So I -- I'm not referring to that.
Q. Okay. So the label as it currently exists for NAION is adequate, correct?
A. Well, I think the verbiage that's in there is certainly an improvement. I think it would -- if -- in the post-marketing section, I think it would be helpful if it included information that they had rechallenge data. I think that the labeling should be more specific that if you have a visual disturbance you should stop the use of the drug. I mean, I -- I think the -- it should probably have a contraindication that if you've been blinded in one eye by Viagra, you should not take the drug again.
Q. Did the FDA request that that information be contraindicated?
A. I don't know. I know it's contraindicated in Europe. I know that Viagra has different labels in Europe than they have in the United States, and there are more significant contraindications in the UK than they have in the United States. Whether FDA required that, I -- I don't know. And I could not find any information where Pfizer attempted to synchronize their U.S. label with the UK, and that the FDA forbade them to -- forbid them to do that.

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MS. LESKIN: Objection; nonresponsive.
JUDGE BORG: Sustained.
BY MS. LESKIN:
Q. Did the FDA ever request that Pfizer contraindicate, in its label, patients with prior NAION?
A. I -- I don't think FDA required that, but that does not --
Q. Did FDA ever request that?
A. I don't know. I don't think so. But nor does that absolve them of the need to -- I mean, really, United States patients and prescribers should have the same information for a product that the European prescribers have.
Q. Are you an expert in European regulatory requirements?
A. No. I've -- we've done some European work. I wouldn't consider myself an expert. But I think that it's appropriate that United States patients have the same benefits that your patients in other countries have.
Q. Did you -- the labeling that currently exists with regard to NAION, that was approved by the FDA, correct?
A. The last label that I have in the report, I believe, is the 2005 label, as far as part of the

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chronology. And then I have the label dated August 2008 juxtaposed to the UK August 2008 label.. But I did not continue the chronology between 2005 and 2008.
MS. LESKIN: Objection; nonresponsive..
JUDGE BORG: Sustained.
BY MS. LESKIN:
Q. The question was: The labeling that currently exists with regard to NAION was approved by the FDA, correct?
A. I thought -- I thought I answered it. I have the FDA-approved label in 2005, but I did not track the FDA approvals between 2005 and what is in here in 2008.
Q. Doctor, I'm not asking you if you tracked it in your report. I'm asking: The label as it currently exists, with regard to NAION, that label was approved by the FDA, correct?
A. And I'm answering you that there's NAION in the 2008 label, NAION information. I did not track it, the 2008 approval, if it were approved label, with what was approved in 2005, so I can't answer your question.
Q. Do you have any basis to believe that there is information in the Viagra label that is not approved by the FDA?
A. Well, certainly they could have added more safety information, more warnings, more

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contraindications, more adverse events without getting an approval from the FDA. They always have the right to do that. I haven't seen evidence that they've done it. But I don't know if there have been subsequent approvals between 2005 and 2008 because I stopped at the time NAION went into the labeling.
Q. Let's talk about the 2005 label..
When the label was changed in July of 2005, that label was approved by the FDA, correct?
A. Yes.
Q. And that label was the result of a prior approval submission, correct?
A. I think that's true. I think FDA required that because they were -- they were standardizing the label among the products.
Q. And FDA specifically required that the draft labeling be submitted as a prior approval supplement, correct?
A. Yeah, because they were -- they were standardizing labeling, yes.
Q. Okay. Now, the FDA was aware of all the various adverse events, ophthalmic adverse events, that we've been talking about today, correct?
A. Oh, I have no way of knowing that.
Q. Well, are you aware of any adverse --

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ophthalmic adverse events that Pfizer did not submit to FDA?
A. I don't know. I did not -- I didn't -- I have no idea if they submitted everything to FDA, nor do I have -- know if FDA was aware of all of these signals that we've discussed. And moreover, doesn't really matter because it's not -- FDA did not at that time have the authority to require that. And it is never FDA's job to maintain the currency, correctness, or adequacy of a company's labeling.
MS. LESKIN: Objection; nonresponsive.
JUDGE BORG: Sustained.
BY MS. LESKIN:
Q. Are you aware of any adverse ophthalmic events that Pfizer did not submit to FDA?
A. I don't -- I don't know either way.
Q. In 2005, when the FDA proposed the label change to include information about NAION, they didn't ask for a label to include information on blindness, did they?
A. I believe they discuss blindness in the NAION information, that it may lead to blindness. I think they did.
Q. But these other events that you've been talking about that cause blindness -- well, let me back up.
There are other causes of blindness besides

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NAION, correct?
A. Yes.
Q. And those other causes of blindness have different mechanisms than NAION do, correct?
A. Yes.
Q. And FDA, when they proposed the label change in 2005, did not suggest lumping all of these ophthalmic events that lead to blindness together to include information about blindness in the label, correct?
A. Well, they note that NAION is a cause of decreased vision and it includes permanent loss of vision.
Q. But they didn't request the inclusion of any other cause of blindness, did they?
A. I'm sorry.. Such as -- such as what?
Q. Such as any other cause of blindness that you've been talking about today..
A. No, they didn't -- they did not include other causes of blindness.
Q. The FDA has medical doctors on their staff, correct?
A. Yes.
Q. And the FDA has ophthalmologists on their staff, correct?
A. Yes.

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Q. And if the FDA -- well, strike that.
MS. LESKIN: Give me a few minutes. I'm just going to go through my stuff and get myself organized.
JUDGE BORG: Yep. We'll take --
THE VIDEOGRAPHER: We're off the video record.
JUDGE BORG: Thank you.
We'll take five.
(Recess from 4:54 p.m. until 5:13 p.m.)
THE VIDEOGRAPHER: We are back on the video record.
BY MS. LESKIN:
Q. Doctor, we were at page 19 of your report. You have a statement here. You make reference to the October 2008 study that started, in the middle of the paragraph.
A. Yes.
Q. Okay. And right after that you have a sentence that reads, "Had a study been initiated when it became apparent (soon after product launch) that ophthalmologic adverse events, many of which were serious, comprised a significant portion of the overall adverse event profile, it is likely the product labeling would contain more stringent language regarding NAION."
Did I read that sentence correctly?

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A. Yes.
Q. Let's go through that piece by piece.
What type of study should have been conducted or initiated soon after product launch?
A. Well, soon -- if we say that it was apparent at 2000, then I would say at 2000. So two years after the launch.
Q. Okay. So --
A. Year and a half. I guess a year and a half after launch.
Q. So that I'm clear, when you say "soon," it's your opinion that a study should have been initiated in 2000?
A. Well, they had events -- we know they had events even the first year they marketed the product, but I -- I mean, it would have been wonderful if they started it in '98, but I picked 2000 because it's a clear -- they had multiple clear signals by 2000. So 2000.
Q. Okay. And what type of study should have been launched -- initiated in 2000?
A. Well, again it would be directed toward the ophthalmic adverse events. And I think it would probably have to be a case-controlled study. I mean, I -- I can think of no way that one can do a prospective

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study with Viagra where we're looking for ophthalmic adverse events and be able to get it through an IRB. Moreover, it's almost impossible to maintain the blind. So --
Q. So when you say an "ophthalmic adverse event," are you saying that Pfizer should have done a study looking at every single ophthalmic adverse event that was being recorded?
A. Well, I certainly think they should -- by 2000 they had reports of temporary and permanent blindness, ION, and NAION, so I think they should have certainly been looking at that cascade of events. And they would have looked at the events, not only comparing the events with a control group, but also an important part of it would be looking to see if within that group there were any particularly vulnerable subgroups.. So the goal would be to quantify the risk, and within the patients, look at those patients who are particular risk of one of those eye events.
Q. And you're saying, though, they should look at any ophthalmic event?
A. No. I was saying that I -- I'm looking at the events related to blindness, temporary or permanent, ION, or NAION.
Q. How temporary is temporary?

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A. I haven't reviewed this with an ophthalmologist.. We'd have to look at -- talk to an ophthalmologist to know the best way to construct that end point in order to study it.
Q. So have you talked to an ophthalmologist as to whether this type of study you're postulating is even feasible?
A. No. I -- no. I have not talked outside -- with any outsiders on this project. I don't think I'm able to.
Q. You haven't spoken to any epidemiologist -- well, strike that.
Have you spoken to any -- any epidemiologist as to whether this type of study is even feasible?
A. Well, Mr. Shearer is an epidemiologist in my office, and we have talked about the study.
Q. Okay. And he's concluded that this is a feasible study?
A. Well, we talked about different designs and the need to do such a study. Yes, he's concluded that, of course.
Q. And how many patients does he say you need?
A. Well, again, that would be dependent on which -- which of the adverse events we were attempting to examine. And we really didn't get to the point that

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we were designing the size of the study. I wasn't asked to do that. But that would be my recommendation.
Q. Have you -- did you talk about how long of a window you would need?
A. No, because I didn't -- I wasn't able to talk to an ophthalmologist. And an epidemiologist -- you need an epidemiologist and a ophthalmologist -- multiple ophthalmologists for that.
Q. Did you determine how long such a study would take?
A. No, because I don't have an appreciation of how quick the patient number is, depending on the number of ophthalmic centers. All of that requires interaction with the actual tertiary ophthalmic centers, and -- and I wasn't able to do that.
Q. Since you haven't spoken with an ophthalmologist, am I correct that you have not spoken with an ophthalmologist as to whether the type of study you have talked about here would provide any meaningful information to an ophthalmologist?
A. Whether information relating to ION, NAION, or blinding would be important to an ophthalmologist?
Q. Well, the study that you've hypothesized here, whether that study would give any meaningful information.

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A. I haven't talked to an ophthalmologist, but certainly the FDA suggested a very similar study, case-controlled studies, examining ION- and NAION-related events. So I think that if the study were properly designed, could be done, properly designed, and gave information, whether good or bad, regarding these adverse events, either outcome would be critically important to an ophthalmologist. I showed you a literature article in 2000 where they were crying for information to be shared with them. So I think that no matter what the outcome, it would have been important to the ophthalmologist, either to warn their patients or to relieve their patients of any concerns. I mean, that's why we do labeling.
Q. You're aware that there was ongoing discussions between Pfizer and the FDA as to the protocol for the current study that is being -- being done about Viagra and NAION, correct?
A. I saw, beginning in 2005 and '6, discussions with them about the protocol, yes.
Q. And some of the discussions that the company had with the FDA was regarding the definition of NAION, right?
A. Well, I think the earlier discussions were that they didn't believe that they could do the study, that

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such a study would not be possible. And after FDA convinced them such a study would be possible, then there were some discussions regarding definition of NAION.
Q. And some of the complications associated with defining NAION, correct?
A. I recall those discussions.
Q. Did the FDA ever ask Pfizer to include the more general term of blindness --
A. I don't know.
Q. -- as part of the study?
A. I don't know.
Q. Did you see that in any of the correspondence you looked at?
A. I did not see that in the correspondence.
Q. Did you see that in any of the minutes of any of the meetings that the company had with FDA about the study?
A. I recall there was a discussion about determining the etiology of any blindness that occurs, but that's all I remember. So I think that FDA was attempt -- was attempting to capture all blinding events.
Q. Really? What document says that?
A. Oh, I just vaguely recall that in reviewing it,

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that they wanted a -- wanted a definition discussion of any events of vision disturbance, vision impairment.
Q. Can you show me the document that says that?
A. No. I just vaguely recall the discussion. But why wouldn't they track that? I mean, certainly they would want to track all their temporary or permanent blinding events.
Q. Doctor, is it your testimony here today that the FDA asked Pfizer to track all blindness as part of this NAION study?
A. No. What I said was, is they asked for a discussion of any reports, discussion to be provided by the investigator of any reports of visual impairment, be it temporary or permanent.
Q. But you don't know what document says that?
A. No. I just recall it when they were discussing with the FDA whether the study could be done.
Q. And you're aware that Pfizer consulted with outside expert ophthalmologists and epidemiologists in developing the protocol for this study, correct?
A. Yes.
Q. Are you aware of whether any of those epidemiologists or ophthalmologists suggested that the generic term blindness be included in the study?
A. I don't know, nor do I know with what proposal

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Pfizer came to them. I don't know if Pfizer asked them whether it would be important to study different types of blinding or if Pfizer went to them and asked them to help them with a protocol design to assess NAION. Two different issues.
Q. Did you look at the documents from those?
A. Yes, and saw that they were discussing a protocol for NAION.
Q. The question was: Did you look at the documents from the meeting?
A. From what?
Q. From the meeting.
A. Yes. My interpretation was, it was a protocol specific to NAION.
Q. That's your interpretation?
A. Yes.
Q. Now, you say here at the end of that sentence, "It's likely the product labeling would contain more stringent language regarding NAION."
What's the basis for that?
A. Well, because Pfizer has continued to receive reports of ION, NAION from -- from 1998 and going forward, so there was no -- was not an isolated event; they've continued to see it. So it is likely that a long-term, a big study, a critically done study, would

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establish the relative risk of NAION with -- with the drug, and hopefully it would show additional information regarding dose-related events, vulnerable subgroup events, length of time.
Q. And you're assuming that the study would show a positive relationship, correct?
A. I'm -- yes. But even if the study didn't show that, that would be well worth to do that study because again the labeling would provide more information for prescribers and their patients.
Q. But if the -- if the study did not have a positive result, meaning show a positive relationship between Viagra and NAION, that the product label would still contain more stringent language regarding NAION?
A. Well, if the study were negative, the labeling would -- may well changed. The labeling would probably still need to include that NAION had been reported in post-marketing adverse events. I don't think there's ever going -- that will ever be removed. But the company could add information that, notwithstanding these post-marketing events, a controlled -- case-controlled study failed to show a difference between the control group. I mean, if that were the case, then NAION would still be in the labeling, but they could add that sentence after, of course.

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Q. So your statement, "It is likely the product labeling would contain more stringent language regarding NAION," that's speculation on your part, isn't it?
A. Well, I think if they did the study, the labeling would change no matter what. It may restrict the NAION warning, NAION precaution, to say, "We've seen it in post-marketing events, but we didn't see it in a case-controlled study, or it may say, "We saw even more, and here are the particular groups." So either way there would be amplified information.
Q. But that's not what you wrote here, is it? You didn't say "amplified information." You said "more stringent language regarding NAION."
A. Yeah. It depends on how the study comes out.
Q. So the fact that the product labeling would contain more stringent language regarding NAION, that's speculation on your part, right?
A. Well, if -- if it restricts the NAION to post-marketing events only, and not shown in a case-controlled study, then that would be more stringent information -- more stringent labeling information, "It's only seen in post-marketing. We didn't see it in a case-controlled study."
Q. And -- and that's what you mean by "stringent" there?

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A. No. I mean it both ways. I have no idea how the study will turn out.. I anticipate it will show that Viagra is associated with significant increased risk of NAION. But until your client elects to do a study, we won't know.
Q. Do you know when Levitra was approved?
A. Yes. It was approved 2003.
Q. And when was Cialis approved?
A. 2003.
Q. Did the FDA request that either -- did the FDA request that the Levitra label include any information regarding NAION?
A. I believe the labeling changed in 2005.
Q. So at the time of approval, did the FDA request that the Levitra label include any information regarding NAION?
A. I don't know, nor do I know if they saw any in their clinical program. I don't know. And I -- and I don't know the rate at which they appeared post-marketing.. I don't know. But notwithstanding the fact that Viagra is the market leader, both -- all of the labelings changed to include that information in 19 -- 2005.
Q. At the time of approval, did the FDA request that the Cialis label include information regarding

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NAION?
A. Oh, it's the same answer. I don't know.
Q. By 2003, the FDA was aware of the reports of NAION in -- so that -- with Viagra, correct?
A. Yes.
Q. Do you have any evidence that Mr. Martin saw any of the Viagra ads that you refer to on page 25 of your report?
A. I have no information about individuals.
Q. Do you have any evidence that Mr. Stanley saw any of the ads referenced on page 25 of your report?
A. I have no patient information at all.
Q. So you just don't know one way or the other whether either of the plaintiffs saw those ads, correct?
A. No idea.
Q. Do you know whether Mr. Martin's physicians saw any of the information regarding --
A. It's the same answer. I have no information regarding individual plaintiffs..
Q. So you don't know what Mr. Martin's doctors or what Mr. Stanley's doctors looked at or relied upon --
MR. BECNEL: Let me enter an objection.
BY MS. LESKIN:
Q. -- is that correct?
MR. BECNEL: Counsel, she was as clear as a

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bell that she has no information on any individual or what they saw or what their doctor saw. Now, how much more repetitious do you have to be?
JUDGE BORG: It's overruled. You -- are you -- do you have a question to the witness?
MS. LESKIN: I did.
JUDGE BORG: Can we have it back?
BY MS. LESKIN:
Q. You don't know what Mr. Martin's doctors or what Mr. Stanley's doctors looked at or relied upon in prescribing Viagra; is that fair to say?
A. I don't know if they saw any of the advertisements, but I know they would have relied upon the labeling in place at that time, and the labeling did not have this information.
Q. How do you know that?
A. Because I understand that the time frame was around 2001 and 2002.
Q. How do you know they read the label?
A. Well, they would have -- you asked what they relied upon. That was the only label, was the one that was in the Pfizer label. And the Pfizer label didn't have it. I'm assuming that that would have been the label they relied upon, since Viagra was a single-source product.

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Q. Did Dr. Martin read any literature other than the label?
MR. BECNEL: Dr. Martin?
MS. LESKIN: I'm sorry.
MR. BECNEL: Dr. Martin? Who is Dr. Martin?
MS. LESKIN: I misspoke. I misspoke.
BY MS. LESKIN:
Q. Did any of Mr. Martin's doctors read any literature other than the label?
A. I don't know.
Q. Did any --
A. I don't know. I have -- okay. I have no information about the plaintiffs or their doctors or their pharmacists.
Q. Does that -- does that also mean that you have no information and you don't know whether Mr. Stanley's doctors read any literature other than the label?
A. Okay. I don't have any information regarding the patients, the doctors, the pharmacists, the pharmacies, and I don't know if anyone read the label.
Q. Well, you made a statement earlier that the doctors would have relied on the label, and the label didn't have information.
A. Right. They would have had to rely on the label because that was the only label available because

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only Viagra marketed the product.
Q. But now how do you --
A. I mean Pfizer marketed the product.
Q. Now you just told me you have no information about the doctor. So which one is it?
A. Oh, my god. I said the same thing ten times. I have no information about the individual plaintiffs or any of their attendings. The only label in effect at that time would have been the Pfizer label. So if they had a -- if the doctors relied upon a label and read a PDR, it would have been the Pfizer label, and the Pfizer label was inadequate.
Q. And you don't know what other information the doctors had available to them; isn't that correct?
A. I -- I don't know what they read. I know what information is available. I summarize much of it in this report. But I don't know what they availed themselves of.
Q. We talked earlier about citizen petitions that had been filed regarding Viagra. Do you recall that testimony, that discussion?
A. Yes.
Q. You know that in 1998 public citizen filed petition -- citizen petition with the FDA to add stronger warnings to the Viagra label, correct?

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A. Yes. I have it on page 12 of my report.
Q. And part of the warning that citizen petition -- that public citizen requested in 1998 was warnings relating to color aberrations, increased light sensitivity, and blurred vision, correct?
A. Correct.
Q. And those events, as far as you know, were related to the PDE6 effect, correct?
A. I think the color events were. I don't know about blurred vision.
Q.. Is there any mention in the citizen petition from 1998 about NAION?
A. I don't think so. The product had just been launched. I don't know.
MS. LESKIN: I'm going to mark as Exhibit 23 a document dated February 28th, 2000.
(Exhibit No. 23 was marked for identification.)
BY MS.. LESKIN:
Q. This is the FDA's response to public citizen, correct?
A. I believe so.
Q. And that's the response to the 1998 petition, right?
A. Yes, I believe so.
Q. If you look at page 8 of the response, there's

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a section entitled "Effects on Vision." Do you see that?
A. Yes.
Q. And the FDA responded by saying, "FDA believes that the Viagra package insert adequately discusses the findings of vision abnormalities and describes the dose relationship associated with these effects," right?
A. Yes.
Q. That was the finding by the FDA in response to the citizen petition in 2000, right?
A. Yes. Well, they also note that the labeling was changed by Pfizer to include post-marketing experiences.
Q. And when was that label changed to include post-marketing experiences?
A. Well, it's been changed a couple times, in '98 -- it was twice in '98. I don't know the dates. FDA says, "Subsequent to your submission of this petition, Pfizer significantly revised the product's package insert."
Q. And on the second page -- I'm sorry, page 9, where they continue the discussion on the vision effects, the FDA noted the adverse reaction section of the label, correct, including the changes made to the post-marketing experience section?

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A. Well, that's where the post-marketing information goes, is in that section.
Q. Right. And they added that there had been reports of diplopia, temporary vision loss, and decreased vision, ocular redness or bloodshot appearance, ocular burning, ocular swelling and pressure, increased intraocular pressure, retinal vascular disease or bleeding, vitreous detachment, traction, and paramacular edema, correct?
A. Yes, all those events were reported post-marketing, correct.
Q. And all of those were added to the label in 1998, correct?
A. That's my understanding.
Q. If you look at page 14 of the FDA's findings, do you see there's a section entitled "Effects of Phosphodiesterase Inhibition on Vision"? Do you see that?
A. I'm sorry. Page?
Q. 14.
A. Okay. I'm there.
Q. Okay. And at the bottom of the page, the FDA writes, "As for the risk of retinal degeneration due to high levels of cyclic GMP, FDA does not believe that there is evidence of such a possibility."

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Do you see that?
A. Uh-huh, yeah.
Q. And that's what the FDA concluded in response to the citizen petition, correct?
A. Based on what was available in 1998, yes.
Q. And all those articles that we talked about before, that was -- those were published before 1998, right?
A. Some were.
Q. Continues on, "The repeated use of Viagra over as much as a -- one year in clinical trials did not demonstrate any serious ophthalmologic adverse events," right?
A. Yes.
Q. And the FDA goes on, "In addition, despite extensive use of Viagra since its approval, FDA has received few reports of serious ophthalmologic adverse reaction.. Consequently, the Agency sees no need at this time to require further labeling changes related to visual problems," correct?
A. Yes. They had already made all the changes you mentioned earlier to post-marketing, so --
Q. And no other changes were necessary as of February 2000, correct?
A. As of, yeah, February of 2000.

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Q. We've talked earlier about the phenomenon of underreporting. You're familiar with that, right?
A. Yes.
Q. And you've said that underreporting is usually between 1 and 10 percent --
A. Yes.
Q. -- correct?
What's the basis for that statement?
A. Dr. Brinker at FDA, last year, testified before Congress and noted that it was 1 to 10 percent.
THE WITNESS: Time?
MR. OVERHOLTZ: Getting really close. It's 5:30 right now.
BY MS. LESKIN:
Q. Do you know what Dr. Brinker's basis for the 1 to 10 percent number is?
A. I think I have the report.
Q. You refer to it on page 7 of your report.
A. I know.
It's a huge report. It's going to take me a minute to find it.
Q. Actually you cite to an FDA presentation --
A. Yes.
Q. -- on December 14th, 2006.
A. I know. But if you're familiar with the

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presentation that they made, it is huge.
Oh, they don't have the speakers in any particular order, so I'm going to have to look for it.
Q. Okay.. But what was the context of the presentation that Dr.. Brinker made --
A. It was a presentation --
Q. You have to let me finish my question --
A. I'm sorry.
Q. -- for the court reporter.
Otherwise she'll get upset.
What was the context of the presentation that Dr. Brinker made?
A. It was a group of FDA employees who were speaking to Congress, to the Institute of Medicine in association with their request for additional funding, and they were requesting additional funding specifically for enhanced authority postapproval. And they were making various -- giving various examples of why they needed this. And it was -- it was needed to do -- was -- so that they would have the authority to require Phase IV studies and the ability to require -- be able to force labeling changes postapproval. And it was secondary to the Vioxx issue and the criticism leveled by Congress on the FDA as a result of the handling of Vioxx.

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Q. Now, you will agree with me that the reporting rate varies from drug to drug, correct?
A. It -- it may, yes.
Q. And some drugs get much more publicity than other drugs, correct?
A. Yes.
Q. And drugs that get more publicity get higher rates of adverse event reports than other drugs, correct?
A. Well, there's a blip after the -- there's a blip after -- during the period immediately after the publicity. But generally you can watch in safety surveillance, and that will -- it will -- the reporting rate will generally go back to a -- to a prior level after the publicity subsides.
Q. Newer drugs tend to get more reports than older drugs, correct?
A. Generally.
Q. Are you familiar with the Weber effect?
A. Yeah, the newness. Yeah. Generally that's true, unless an older drug has -- new information is made available about the newer drugs -- I mean, I'm sorry, about the older drugs.
JUDGE BORG: The older drugs. Right. I don't mean to correct the witness but --

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THE WITNESS: I caught it.
JUDGE BORG: I know what you meant. You caught it.
THE WITNESS: I caught it.
BY MS. LESKIN:
Q. And serious events get more reports than nonserious events?
A. Generally that's true if they're -- if the physicians can discern -- can tease away from the patient's -- otherwise the patient's condition. That's generally true, for a period.
Q. And litigation increases adverse event reporting, correct?
A. Again, there's usually a phasic period, a blip period; and then it goes back down to a baseline level.
Q. Do you know how many of the adverse events in the Viagra database for NAION are litigation reports?
A. No.. I stopped at 2004.
Q. Do you know how many of those reports are litigation reports?
A. No, no.
Q. Now, you -- going back to page 7 of your report, you say, "Several factors contribute to the low percentage of significant adverse medical events actually reported to FDA and other authorities."

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Do you see where I am?
A. Yes.
Q. Okay. Let me just take you to that sentence right above it, which is the last sentence on the prior paragraph. And you said, "It is thereof imperative that manufacturers closely monitor all available data, conscientiously review published literature, conduct necessary follow-up studies, and fully explore all potential adverse events."
A. Yes.
Q. Do you have any evidence that Pfizer did not do that?
A. Well, I don't think they conducted a follow-up study in a timely fashion, and I don't think they amplified the labeling as a result of the ophthalmic-related events we've discussed today.
Q. Did Pfizer closely monitor the available data to them?
A. I haven't -- I haven't offered an opinion in my report that they didn't. I don't know.
Q.. Did Pfizer review the published literature?
A. I don't know. I don't know. My report focuses on the fact that no action was taken, not that they didn't know about it. I'm assuming they knew about it.
Q. Well, specifically that they didn't change the

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label when they did not initiate a case-controlled study, correct?
A. Or any study. Or any study to examine it. I mean, I didn't see any records that they attempted to do a cohort study either.
Q. And those are the only two types of studies that would have answered the question, to you?
A. There's other studies that one can do, it's just I was attempting to look at ones that might be more readily doable. I think a prospective double-blind controlled study with this drug and these events would be difficult to execute. I didn't see any evidence that they attempted it to look at this adverse event, but I think it would be difficult to execute.
Q. On page 8 you say one of the other factors contributing to a low reporting rate, you write, "If a manufacturer inaccurately, incompletely, or inarticulately submits adverse event reports and subsequent analyses, the FDA may not fully appreciate an emerging or changing safety profile associated with a drug product."
Do you see that sentence that you wrote?
A.. No. Could you --
Q. Sure.
A. -- repeat where?

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Q. Page 8 --
A. I got distracted.
Q. Sure. Page 8, the top full paragraph.
A. Yes.
Q. In the middle of the paragraph, you have a sentence that reads, "If a manufacturer inaccurately, incompletely, or inarticulately submits adverse event reports and subsequent analyses, the FDA may not fully appreciate an emerging or changing safety profile associated with a drug product."
Did I read that correctly?
A. Yes.
Q. Do you have any evidence that Pfizer inaccurately submitted adverse event reports?
A.. I don't recall seeing in their periodic reports an analyses of the escalating events of ION, an evaluation over time of the escalating events of ION in the various databases. I don't -- I did not see an overview from adverse event databases, the literature where they did a signal analysis and submitted that to FDA.
Q. Do you have any evidence that Pfizer inaccurately submitted adverse event reports to FDA?
A. Yeah, I -- I didn't see analyses of these events. I saw events reported, but I didn't see a

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distillation or an analyses of these over time and sharing with the FDA that they believe that a signal had -- had been obtained in 2000 and maintained until 2005.

Q. Is anything about the adverse event reports that were submitted to FDA inaccurate?

A. The individual reports?

Q. Yes.

A. I didn't specifically look for invalidity in the individual reports. I was more concerned with an analysis overview. But -- but I -- I have not said that they lied or submitted anything inaccurately in the individual reports. I just didn't see an overview analysis of the events during that -- that time period.

Q. So you're not offering an opinion that FDA at all -- I'm sorry.

You're not offering an opinion that Pfizer misled the FDA; is that fair?

A. I didn't see information where Pfizer brought the issue to the FDA during the 2000 and 2005 time period, but I'm not saying that they lied to the FDA. I didn't see that they gave a complete overview to the FDA, though.

Q. But your opinion in this case is not that Pfizer lied to FDA, correct?

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A. No, I don't think I've said that Pfizer lied to FDA.

Q. And your opinion in this case is not that Pfizer withheld information from FDA, correct?

A. I didn't see an analyses where they did the type of analyses --

Q. Okay.

A. -- that we've discussed.

I didn't see it.

MS. LESKIN: Objection; nonresponsive.

JUDGE BORG: Overruled.

BY MS. LESKIN:

Q. And maybe I wasn't clear.

Are you offering an opinion in this case that Pfizer withheld information from the FDA?

A. It's the pharmaceutical company's responsibility to track information and make labeling changes. I didn't see where Pfizer attempted to make a labeling change to address the escalating events that we've discussed today with FDA.

Q. You've said that now twice, Doctor. And I'm -- I'm not asking what you think the company didn't do, except I'm asking: Did the company withhold information that it had from the FDA?

A. I don't know how else to answer it.

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I didn't see a synthesized report of these events between 2000 and 2005. I didn't see that the company did anything with respect to discussing this with FDA prior to FDA forcing the actions. So I didn't see those reports.

But I didn't say they lied on individual events. But I didn't see any effort or energy being made to -- to get this information as they received it into the labeling, and then modifying it as additional information became available. I saw nothing till the FDA was involved in 2005.

Q. What information did Pfizer have that they did not give to FDA?

A. It isn't enough to simply give individual reports and give counts. A company is required to assess, address, evaluate the information overall. I didn't see that. And I think that the information we've discussed today from these various databases provided an overview of events that were occurring, and I think it required a labeling change earlier than 2005..

JUDGE BORG: I think you have four or five minutes left, Ms. Leskin. Two? Two minutes.

MS. LESKIN: Thank you.

BY MS. LESKIN:

Q. Did you see any information that Pfizer did the

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analysis you think they should have?

A. I didn't see an overall analyses of the data between 2000, 2005. I saw where they reviewed events as they occurred, but I didn't see a pharmacovigilance assessment of these events across the various data sources during this time period.

Q. The time period being between 2000 and 2005?

A. Yes.

Q. Other than this information, this analysis that the company did not do, is there any other information you believe that Pfizer did not give to the FDA?

A. Well, I think if Pfizer had done this analysis, or whether they did or didn't do it, they should have provided for labeling changes during this time period.

Q. But did they withhold anything else from the FDA that they had?

A.. Well, that's all I've addressed. My interest in this was the ophthalmic reports during these time periods for Viagra only. I didn't address other issues with Pfizer in this report.

MS. LESKIN: You can change the tape.

THE VIDEOGRAPHER: We are not out of tape.

MS. LESKIN: Oh.

JUDGE BORG: It's not the tape we're out of. You're out of seven hours.

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MS. LESKIN: Okay. Let's take a break off the record.
THE VIDEOGRAPHER: We're off the video record.
(There was a discussion off the record.)
THE REPORTER: Am I supposed to be on the record? Because I am not.
JUDGE BORG: Do you all want this on the record?
MS. LESKIN: Yes.
THE REPORTER: I'm going back on now.
MS. LESKIN: I'm representing that I have five minutes or less of time left. I've asked for an agreement of counsel. They've refused to provide agreement.
I am now appealing to Judge Borg and asking that in light of the extended colloquy that went on on the record, including on the videotape, including time that the witness was out of the room, that I be given an additional five minutes to be able to complete my examination.
MR. BECNEL: Ms. Leskin, in answer to your request, you have been so repetitious throughout this deposition over and over, and wasted time asking the same question over and over, when the witness has given you answers, you could have gotten

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your five minutes.
The problem is, if you recall, when you objected to virtually every single question asked of Dr. Hayreh or objecting to everything he was doing, you know, we didn't get that courtesy. So I don't intend to give you that same courtesy.
MS. LESKIN: Dr. Hayreh was your witness.
MR. BECNEL: Yeah. But you made --
MS. LESKIN: I was taking his deposition.
MR. BECNEL: -- most of the objections to everything he said.
JUDGE BORG: Well, she -- well, okay.
You can have five more minutes because of the discussion on the record without the witness present. And the -- and the Court's order for deposition says seven hours of examination, and that was not examination. So you get five more.
We're back on. Can you -- are you ready to proceed, Ms. Leskin?
MS. LESKIN: I'm sorry?
JUDGE BORG: Are you ready to proceed now?
MS. LESKIN: Yes.
THE VIDEOGRAPHER: One moment, please. Let me get rolling.
We are back on the video record.

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(Exhibit No. 24 was marked for identification.)
BY MS. LESKIN:
Q. Dr. Blume, I'm going to hand you what's been -- we've marked now as Exhibit 24. I'll represent to you that Dr. Osterloh, at his deposition, confirmed that this was a report he prepared and submitted to the EMEA in 2002.
Did you ever see this document before?
A. I think so.
Q. And did you review this document in reaching your opinion in this litigation?
A. I -- yes, I think I reviewed this.
(Exhibit No. 25 was marked for identification.)
THE WITNESS: I'm sorry. Who did you say? Osterloh, right? Yes. This is -- yes. This is an in-house report. Yes.
BY MS. LESKIN:
Q. Well, are you aware that this was a report that was submitted to the EMEA?
A. Yes.
Q.. So it's not an in-house report?
A. Well, it was compiled by the in-house --
Q. Okay.
A. -- staff.
Q. I'll give you a document numbered Exhibit 25,

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which is a document dated December 6th, 2002, by Jeanette Barrett, also with Pfizer. I'll represent to you that at Dr. Osterloh's deposition, he confirmed that this report is part of the submission made to EMEA in 2002.
Have you seen this document before?
A. I thought I had cited it.
Q. Okay. And so you reviewed this document in connection with your report, correct?
A. I cited this. Yes.
MS. LESKIN: Okay. I have nothing further. Thank you very much, Doctor.
JUDGE BORG: Mr. Overholtz or whoever, are you going to do the exam?
MR. OVERHOLTZ: We're going to take a break and --
JUDGE BORG: Well, I was going to do that, but I was going to ask if you wanted a break.
MR. OVERHOLTZ: I think Mr. Altman is going to ask some questions, then I'm going to ask some questions. Okay?
THE VIDEOGRAPHER: We're off the video record..
(Recess from 6:00 p.m. until 6:13 p.m.)
THE VIDEOGRAPHER: We are back on the video record.

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BY MS. LESKIN:
Q. Dr. Blume, I just need to make a correction on the record. I -- we marked as Exhibit 25 a report prepared by Dr. Barrett dated December 6th, 2002, and I think I represented to you that that was submitted to EMEA.
If you look at the first paragraph in the abstract, it says that the report has been prepared in response to questions posed by the Swissmedic.
A. Uh-huh.
Q. So I apologize. I didn't mean to mislead you.
MS. LESKIN: Let me mark as Exhibit 26 a report by Ms. Barrett -- Dr. Barrett dated June 28th, 2002.
(Exhibit No. 26 was marked for identification.)
BY MS. LESKIN:
Q. And you'll see in the first paragraph that this report was prepared in response to a question posed by the rapporteur from the Dutch Medicines Evaluation Board, and that that was submitted with Dr. Osterloh's report to the EMEA.
So have you seen this document that we marked as Exhibit 26 before?
A. Yes.
Q. I'm sorry. Yes?
A. I said yes.

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Q. Okay. Thank you very much.
MR. OVERHOLTZ: This is the same -- are you talking about the same document or a different document? Did you replace it?
MR. ALTMAN: No.
MS. LESKIN: No.
MR. ALTMAN: New exhibit.
MS. LESKIN: I gave her the one June 28th, 2002. It's a different --
MR. ALTMAN: This is Exhibit 26.
MS. LESKIN: One is dated December and one is dated June.
MR. OVERHOLTZ: It was -- this was 25, and this is now 26?
THE WITNESS: Yes.
MS. LESKIN: Correct.
MR. ALTMAN: Well, they're not -- it just appears they're not exactly the same document. The other one appears to have more pages. So I don't know what the difference is between the two.
MS. LESKIN: They're two different reports.
JUDGE BORG: They're two different reports.
MR. OVERHOLTZ: Two different reports and different days and everything.
MR. ALTMAN: Okay. All set?

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MS. LESKIN: I'm all set. Go for it.
CROSS EXAMINATION
BY MR. ALTMAN:
Q. Dr. Blume, I just have a few questions on -- for you.
I want to go over your background very briefly.
How long have you been working in the pharmaceutical industry?
A. Since 1977.
Q. And while working in the pharmaceutical industry, have you held any supervisory or management positions within a pharmaceutical company?
A. Yes.
Q. Can you just tell us those positions very quickly?
A. Yes. I have been a technical director, vice president of scientific affairs, chief operations officer. I've been a member of the board of directors.. And that's it.
Q. And which companies was that for?
A. I worked for both Mylan Laboratories and for Somerset Pharmaceuticals.
Q. When you were at the pharmaceutical companies, did you have responsibility for the assimilation, shall we say, of information from lots of different sources in

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rendering business decisions and safety decisions?
A. Yes, of course.
Q. Okay. In your either a capacity while at the pharmaceutical companies or in your consulting capacity afterwards, do you develop INDs?
A. Oh, yes, yes.
Q. More than one?
A.. Yes, multiple ones. Yes.
Q. Do you develop new drug applications?
A. Yes.
Q. When you develop INDs in your drug applications, do you have substantial authorship responsibilities for those applications?
A. Yes. For -- for most of those I am the U.S. -- U.S. contact for our clients with the FDA.
Q. Do you assimilate all the -- much of the information that would go into those NDAs and INDs?
A. Yes.
Q. And do you prepare the overall structure?
A. Yes.
Q. Do you develop the integrated summary of safety for those NDAs?
A. I develop both the ISS, integrated summary safety, and the ISE, the integrated summary of effectiveness.

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Q. As part of your experience, do you draft labels?
A. Yes.
Q. Have you had primary responsibility for drafting the label from scratch, shall we say?
A. Yes. A new label associated with a launch NDA?
Q. Yes. Have you had responsibility for negotiating the language of draft labeling with the FDA?
A. Yes.
Q. Have you had primary responsibility for making changes to a label subsequent to the initial marketing?
A. Postapproval labeling?
Q. Yes.
A. Oh, yes, yes.
Q. Have you ever, of your own volition, suggested to the FDA that a labeling change needed to be made?
A. Yes. I've submitted -- independently submitted both labeling changes requiring approval and affected labeling changes that didn't require prior FDA approval.
Q. In your capacity, your consulting capacity, have you developed clinical trials?
A. Yes.
Q. Have you selected -- help select the organizations that conduct the clinical trials?
A. Yes. Contract research group, yes.

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Q. Have you had responsibility for collecting the information from the clinical trials and simulating that into the overall new drug application or IND?
A. Yes. The information from the trials are -- are provided, and it's my responsibility to develop that into a new drug application format.
Q. With respect to the INDs, the NDAs and the labels, and the ANDAs, are you just simply signing off on these applications or are you actually -- does the buck stop with you in many of these applications?
A. No. When I was in industry, I was responsible for the departments for securing NDA approvals. And in my capacity here, PDG works with companies in all -- in all facets of their NDA preparation. But in the NDAs that we have submitted for our clients, I am the contact, I am the one responsible for the preparation and the approval, getting -- securing the approval of the NDA.
Q. And do you, as part of that capacity, negotiate the approval process with the FDA?
A. Well, I'm -- I'm the one who attends the meetings with FDA prior to submission of the NDA to make sure that we agree upon what the format will be and what data will be submitted, and I am responsible for coordinating the answers of approvable letters or

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deficiency letters during the FDA review process and securing the final FDA approval.
Q. And do you -- do you correspond regularly with the FDA in this capacity?
A. Oh, yeah.
Q. Okay. I want to ask you just a few general questions.
Do you know what I mean by the term "clinical signal"?
A. Yes.
Q. As a -- and that would be something different than a data mining signal, correct?
A. Yes.
Q. Okay. Can you disprove a clinical signal through the use of data mining?
A. No.
Q. Okay. I'd like to hand you --
MR. ALTMAN: What's the next exhibit?
THE WITNESS: 27.
MS. LESKIN: 27. There's a sticker here for you.
(Exhibit No. 27 was marked for identification.)
MR. BECNEL: This one?
MR. ALTMAN: Yeah.
BY MR. ALTMAN:

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Q. This is a paper entitled "The Potential Utility of Data-Mining Algorithms For Early Detection of Potentially Fatal/Disabling Adverse Drug Reactions: A Retrospective Evaluation."
Have you ever seen this paper before?
A. Oh, yes.
Q. Are the authors of this paper Manfred Hauben and Lester Reich?
A. That's correct.
Q. If you look at the bottom, right above the page number on the first page, does it say there that this document comes from Pfizer?
A. Yes.
Q. Okay. And Dr. Hauben works for Pfizer, correct?
A. Correct.
Q. Okay. Would you -- I'd like you to read about -- one, two, three, four, five, six, seven -- eight lines down starting with the sentence that says "Pharmacovigilance," do you see that, "is dependent"?
A. Yes.
Q. Okay. Would you please read that?
A. "Pharmacovigilance is dependent on astute clinical recognition of an unusual or unexpected pattern of events or a pattern of events that is consistent with

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a biologically plausible explanation, either within a single case or across a series of cases."
Q. And just read one more sentence.
A. Uh-huh. "Such clinical/pharmacological knowledge-based approaches have been referred to as traditional methods of signal detection."
Q. The -- the mechanism that was just described here in this paper, is that effectively the same mechanism as you use in conducting your pharmacovigilance activities?
A. Right.
MS. LESKIN: Objection. I don't think there's a method defined in this paper.
JUDGE BORG: I'm sorry. What's your objection?
MS. LESKIN: It's vague.
JUDGE BORG: Overruled.
Do you understand the question? Are you able to answer?
THE WITNESS: Yes.
JUDGE BORG: Okay. Go ahead.
MR. ALTMAN: Okay.
BY MR. ALTMAN:
Q. Dr. Blume, I'd like you to take what was marked as Exhibit 9 previously.
A. 9?

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Q. Yes. That's the June 15th, 2000 letter from Pfizer to the editor of Ocular Surgery News.
Well, you know, for ease of finding it, I'll just hand you this one.
A. I found it. There we go. Okay.
Q. Dr. Blume, would you -- is it your opinion that this document represents that Pfizer had recognized a -- Pfizer had a signal as of June 15th, 2000?
A. Yes, yes.
Q. With respect to the last sentence, "We will continue to follow with care the information being collected by Drs. Egan and Pomeranz."
Did I read that sentence correctly?
A. Correct.
Q. Does that demonstrate to you that Pfizer recognized that they needed to do some monitoring based upon the signal?
A. Yes.
Q. We looked at the chart. I don't remember what exhibit number you marked it as. That was the chart from the AERS database.
A. 10.
Q. Okay. Would -- would a difference of a few reports through there, which could possibly be data entry by the FDA or duplicate by the company, would that

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substantially change that chart?
A. No, because the -- the same pattern was seen on several sequential years. No.
Q. Okay. Is there any rule that says internally a company has to use any particular database for how it describes adverse events?
A. No. Companies are encouraged to use as many databases as they can. In fact, when FDA now communicates with you on what they want in INDs and NDAs, they list several and then offer for you to offer additional ones to them. But AERS is always included.
Q. I think I asked a slightly different question.
In terms of describing an adverse event, the terms to use, is there any requirement that a company use any particular dictionary internally in describing those adverse events?
A. No.
Q. Okay. Have you ever heard the term "COSTART"?
A. Yes.
Q. What is COSTART?
A. A dictionary of terms to proceed -- was used previously.
Q. When you say "previously," is that previously to MedRA?
A.. Yeah, prior to MedDRA.

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Q. I think the question was asked earlier about the FDA using WHO-ART. Did the FDA ever use WHO-ART?
A. Yeah, I didn't quite understand that either. No.
MR. BECNEL: Ms. Reporter, is he going a little too quickly for you here?
THE REPORTER: Yes. Could you slow down a little?
MR. ALTMAN: Absolutely.
MR. BECNEL: Please don't be shy about that.
MR. ALTMAN: You've got to throw something at me.
MR. BECNEL: This is New Yorkers. This is New Yorkers. That's what they do.
JUDGE BORG: Well, it's going to be a hard enough transcript as it is, so.
BY MR. ALTMAN:
Q. With respect to the 2005 citizen's petition by public citizen, did you review that document before drafting your expert report?
A. Oh, yes.
Q. The Exhibit 10, is that anything other than just a breakdown by year of the same adverse event reports that were part of the public citizen citizen's petition?

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A. Yes, exactly. It's the same database, but instead of doing the cumulative, it's a breakdown by year.
Q. Okay. When you look for signals, whether clinical or data mined, do you limit it to just one specific term or do you use collections of terms together that may have similar properties?
A. No. You really -- it's almost impossible to limit it to a single term because prescribers -- many people submit adverse event reports, prescribers, hospitals, insurance databases, and the terminology may vary. So it's important when trying to focus on a particular concern, a particular adverse event that you attempt to access as many descriptive terms as possible when coming to a conclusion if there is a signal or if that signal has changed.
Q. And what you've just described there, is that the way you've conducted pharmacovigilance in your regulatory activities while you were at industry?
A. Oh, yeah. That's the way we have to. Yeah.
Q. I'd like you to pull your expert report for one second. And could you please go to page 13.
In the first paragraph that starts "while Pfizer," there was some questions about those three documents that are listed as part of that sentence.

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A. Yes.
Q. Now, there are two clauses of that sentence. One is that Pfizer was aware of NAION cases in 2000, correct?
A. Right.
Q. And the other one is that their response seemed to focus on deflecting negative publicity, correct?
A. Correct.
Q. Do those three -- can those three documents that are listed apply to one or both of those clauses?
A. Yes.
Q. Okay. So you weren't necessarily saying there that all three of those were specific for deflecting negative publicity, correct?
A. No. I think the first two of those was confirmation that Pfizer had to -- was aware of the NAION cases as early as 2000.
Q. We talked, I think with Dr. McGwin's report, about statistical significance. Does a lack of statistical significance mean that you conclude that there is no effect?
A. Oh, no, never.
Q. Okay. Do all -- do all -- strike that.
Does the FDA require a manufacturer in the United States to submit all adverse event reports to the

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FDA?
A. No.
Q. Do foreign-labeled adverse events have to go to the FDA?
A. No.
Q. Do foreign nonserious events have to go to the FDA?
A. No.
Q. So even if complying with the regulations, is it your opinion that the -- that the company would have more adverse event information than the FDA would have in terms of events that went to the company?
A. Oh, for their product, the company always has more information than the FDA, always.
Q. So if the company had --
JUDGE BORG: Mr.. Altman, slow it down --
MR. ALTMAN: Sorry.
JUDGE BORG: -- a little bit, please.
BY MR. ALTMAN:
Q. Sorry. If the FDA has -- strike that.
If the company had more information than the FDA, can the FDA on its own replicate an analysis that the company could do?
A. No.
Q. Is there any requirement that the company do

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more than simply collect adverse event reports and submit them to the FDA?
A. Yes. And I -- and I was describing that a little earlier. If you look at the regulations in -- outlined in 314.8, it isn't -- it isn't sufficient to simply list the events and send them to FDA, a tabular listing. One has to assess, analyze, evaluate your adverse event reporting. So FDA relies upon you to do the evaluation of all these different sources of information that only the manufacturer of the product can access.
Q. Does the company have to prove a causal relationship in order to make a labeling change?
A. No, not at all. FDA is very specific about that you do not have to.
Q. Does the company -- does the FDA require proving a statistically significant association in order to make a labeling change?
A. No. In fact I mentioned one of my labeling changes based on two adverse events.
Q. To your knowledge, has anybody ever written or opined about the importance of a single rechallenge event?
A. Yes.
Q. Can you tell us some of the sources of where

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you read that or heard it or seen it?
A. At -- Dr. Goldman has -- from the FDA has opined on that. And I believe Dr. Hauben has mentioned it.
Q. Dr. Hauben is?
A. From Pfizer, has mentioned the importance of even one documented rechallenge report.
Q. You're not -- we discussed before, you're not a clinician, correct?
A. Correct.
Q.. But in your 30 years of experience, has it been your day-to-day responsibilities to interpret clinical information and how to convey ramifications of clinical information to -- through labeling or to interpret or make decisions based upon clinical information?
A. Yes. I design clinical trials. I summarize the data from clinical trials for FDA's purposes. And I -- and I write the labeling relating to the clinical trial data.
Q. And while you would not necessarily diagnose a patient in terms of an adverse event, do you interpret the information provided in adverse events in terms of how -- whether that is adequately labeled or a labeling change should be made?
A. Yes, yes.

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Q. And as a part of your practice, do you take collections of disparate information from many different sources, whether it be clinical trials or post-marketing safety surveillance or the literature or from wherever, and assimulate that information into a cohesive picture so that you can make a decision or recommendation?
A. Yes, routinely.
Q. Have you made labeling changes or recommended labeling changes based on that kind of activity?
A. From multiple sources of information?
Q. Yes.
A. Yes.
Q. Okay. And I just have one last question for you before I pass you to -- to Neil.
Are there any opinions that you've rendered in this case that are not of the type of opinions that you render on a regular basis outside of the context of litigation?
A. Right. The assignments that were conducted in evaluating the data in this report are -- are very similar to the assignments that we are required to do while assessing a product's worthiness to submit for approval and whether when we assess post-marketing data with a product that's been launched and/or conducting -- developing our periodic safety update reports or

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deciding on whether to make labeling changes relating to new safety information. It's the same type of assignment.
Q. And the methodologies that you used to write -- to render your opinions in the report are the same as the methodologies that you use every single day?
A. Yes. The methodologies that we have used in new drug development are the same as what we use in litigation, and the information and the steps that I take with literature and evaluation of post-marketing clinical study reports are exactly the same.
MR. ALTMAN: Pass the witness.
MR. OVERHOLTZ: Thank you.
CROSS EXAMINATION
BY MR. OVERHOLTZ:
Q. Dr. Blume, I have a few questions for you, and I want to start out by following up on questions Keith was just asking you.
It's your opinion that a pharmaceutical company has a duty to conduct pharmacovigilance for their products?
A. Yeah. They're required to conduct it, yes.
Q.. And by conducting pharmacovigilance, can you tell the jury what you mean by what duty the pharmaceutical company has?

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A. Right. Prior to approval, a limited -- there's only a limited amount of information available to a company regarding a new product. And there's two reasons for that. One is that the clinical trials are often only four to ten thousand patients, and many of those patients -- and several of those patients can receive placebo therapy; and moreover, as we've discussed today, the patients that are used in a clinical trial for NDA purposes are generally as clean a population as we can have, in order to study the particular drug effect.
So for both of those reasons, we learn the real safety information about a product after the product has been approved, because then it goes into hundreds of thousands or millions of patients, and it's in a real-world setting where patients will be given the drug that weren't allowed to have the drug prior to approval and who take the drug in ways outside the labeling provision. So that's when we learn safety information. And that's why we have to do pharmacovigilance. Many of the events that we learn could not have -- could not have been realized in our clinical trials.
Q. Okay. Within the pharmaceutical industry, are there accepted methodologies for conducting pharmacovigilance?

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A. There are. But pharmacovigilance is largely dependent on your patient population and on the drug product and of the event of interest. So oftentimes pharmacovigilance is tailored by a company for their particular product and their particular concern with that product.
Q. And tailoring the pharmacovigilance activities that a pharmaceutical company would undertake is part of the regular practice of pharmaceutical companies in the industry?
A. Oh, absolutely, absolutely.
Q. Now, in reaching your opinions that you stated in your expert report, did you use the same accepted methodology that you would use in your profession working for pharmaceutical industry?
A. Yes.
Q. And in reaching the opinions that you've stated at your expert -- at your deposition today, did you apply this same accepted methodology regarding pharmacovigilance in coming to those opinions and stating those opinions?
A. Yeah.
Q. And does a pharmaceutical company have a duty to comply with regulatory obligations?
A. Yes.

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Q. And in reaching your opinions that you've stated in your report in analyzing Pfizer's compliance with the regulatory obligations, did you apply the same standards and same methodology you would -- that you would apply to a pharmaceutical company that you were working for in your profession?
A. Yes.
Q. You remember you were asked some questions on direct about the fact that -- and there were many documents where Pfizer indicated that they were aware of no adverse events of NAION-related adverse events in their clinical trials. Do you recall those documents and questions?
A. Yes.
Q. Okay. In light of that information, before going to market with the drug, would Pfizer have expected to see an excess of adverse events for NAION?
A. Well, they did not see any in their clinical trials, I believe, so they would have had that background information. However, they should have been looking, I think, or should have -- should have been aware of the retinal effects and the hypotensive effects of the drug. So the hypotensive properties of the product were well known, well established in the labeling.

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Q. I asked you about pharmacovigilance.
Pharmacovigilance allows a company to detect a signal regarding a potential safety issue with the drug?
A. That's one of the reasons one does pharmacovigilance, yes.
Q. And you told Mr. Altman that you believe that Pfizer by 2000, with the Pomeranz reports, had received a signal related to ischemic optic neuropathy in Viagra; is that correct?
A. Well, yeah. That -- in fact that article was said -- they said that they see it and they're going to monitor it.
Q. And in giving the opinion that Pfizer had reached a signal based on -- should have received a signal based on pharmacovigilance, you reached that opinion applying the same methodology you would apply to a pharmaceutical company that you've worked for in your profession?
A. Yeah. Yes, of course.
Q. Do you agree with the statement that a company has a duty to investigate a signal?
A. Oh, yes.
Q. And if a company begins an investigation of a signal, and through that investigation concludes that they are unable to exclude their drug as a cause of a

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serious adverse event, does the company have a duty to warn about that event?
A. That they're unable to exclude their drug as a cause?
Q. Yes.
A. Well, yeah, of course.
Q. In other words, a company that reaches that conclusion that they can't exclude the product as a cause after investigating a signal, should that company amend its product labeling to warn physicians?
A. Of course, yes.
Q. And so if Pfizer concluded that they could not exclude Viagra by 2002 as a cause of reports of NAION, should they have amended their labeling and warned of NAION?
A. Yes, sir. In my opinion, certainly.
Q. I show you what was marked as Exhibit No. 24. If you could pull that up. And it's previously marked as Exhibit 24.
A. I have it..
MS. LESKIN: Can I have it? What was that?
MR. OVERHOLTZ: I don't know where it went.
MS. LESKIN: What was it?
MR. OVERHOLTZ: "Sildenafil and Anterior Ischemic Optic Neuropathy."

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THE REPORTER: I'm sorry, say that again.
MR. OVERHOLTZ: "Sildenafil and Anterior Ischemic Optic Neuropathy." It's the one that's Bates 003 283877.
MS. LESKIN: I got it.
MR. OVERHOLTZ: Okay.
MS. LESKIN: Thank you.
BY MR. OVERHOLTZ:
Q. AND this was the report that Ms. Leskin showed you that she indicated that Osterloh had testified had been provided to the EMEA regarding the reports of NAION. Do you recall that?
A. I do.
Q.. If you could turn with me over to page 6, there's a paragraph. Do you see that?
A. I do.
Q. And it says -- it starts with "In conclusion."
A. I see it.
Q. Okay. And if you could read for me the last sentence, that begins with "However."
A. "However, due to the nature of spontaneous case reports it is virtually impossible to definitively -- to -- yeah, definitively exclude any causal link, and so it is important to continue to review new reports of cases and new clinical studies and periodically reassess

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this issue."
Q. Okay. In light of that statement, do you believe that Pfizer had a definitive signal of NAION by 2002?
A. Yes.
Q. And based on that statement, should Pfizer have warned of NAION?
A. Yes, I believe so.
Q. Doctor, you were asked some questions by Ms.. Leskin regarding whether the Martin -- Mr. Martin, Mr.. Stanley saw Viagra ads. Do you recall those?
A. Yes.
Q. Have you seen a Viagra ad on TV?
A. Yes.
Q. Do you know anybody with a television that hasn't see a Viagra ad on TV?
MS. LESKIN: Objection. Outside the area -- outside her expertise.
JUDGE BORG: I'm going to overrule it.
BY MR. OVERHOLTZ:
Q. Go ahead, you can answer.
A. I don't know how they could miss it.
Q. Okay. Viva Viagra. We can sing along if you wanted to, right?
Is it your opinion in this case that Pfizer

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should have warned of permanent vision loss associated with Viagra by 2002?
A. Yes. Reported with Viagra, yes.
Q. You were asked some questions regarding changing a label?
A. Yes.
Q. And I want to kind of clarify something.
As a company learns more information regarding the specific nature of an adverse event and its association with the product, is it -- can the label be revised to reflect this more accurate information that the company has learned?
A. Yes, of course.
Q. So as -- if Pfizer would have initially warned of -- of permanent vision loss in their labeling for Viagra when they saw a signal, as they -- as they received more information regarding that association, they could have revised the label to add additional information?
A. Well, of course. We call the labeling a living organism because it's always changing.
Q. Do you recall some questions on direct regarding the terms of coding for NAION?
A. Yes.
Q. And was your testimony that NAION was not a

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term that was available to Pfizer --
A. That's correct.
Q. -- and coding to the -- as far as with -- in the AERS database --
A. That's not true.
Q. -- of the FDA.
Instead, it had to be coded to terms like ION or optic neuritis or blindness --
A. Blindness, correct.
Q. -- is that correct?
A. That's correct.
Q. Okay. In light of that fact, would it be reasonable for a company looking to investigate NAION associated with their drug to review all adverse event reports in their database that could potentially be a NAION case?
A. Oh, yes, of course.
Q. In other words, it would be important to look at any adverse event reporting a sudden loss of vision. Is that -- would that be a fair statement?
A. Yes, yes.
Q. And any reports of blindness?
A. Correct.
Q. And that's because blindness -- NAION can result in blindness --

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A. Right.
Q. -- is that right?
A. Correct.
Q. Okay. And in fact in 2005, are you aware as to whether or not the FDA asked Pfizer to review their adverse event database for a broad range of terms associated with NAION?
A.. Yes. I think it was mentioned that they gave a complete list of term -- terms in an effort to trap all possible ways of describing the events of interest.
Q.. Do you recall testimony that you gave earlier regarding the 1998 label change that added entry regarding temporary decreased vision or vision loss?
A. Uh-huh, yes.
Q. Okay. By 1998, Pfizer had also received reports of permanent vision loss?
A. Correct.
Q. They had received reports of ION; is that correct?
A. Correct.
Q. By 1999, was that -- the same true?
A. Right.
Q. They -- by '99 they received reports of permanent vision loss?
A. Yes.

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Q. By 2000, had Pfizer received such reports?
A. That's true.
Q. The same would be true for 2001 and 2002?
A. Right.
Q. All the way through 2005?
A. Correct.
Q. Was it reasonable for Pfizer to not amend its label to add permanent vision loss to the labeling for Viagra between 1998 and 2005 in light of the fact they had received a growing number of reports of permanent vision loss?
A. Yes. I think that section should have been amended to include both temporary and permanent blinding.
Q. And was it -- was it reasonable for Pfizer to not add ION as an adverse event under the post-marketing surveillance report as they had added earlier the '98 change regarding temporary vision loss?
A. Right. That should have been added as well.
Q. Should have been added by 1999?
A. For 2000, yes.
Q. By 2000?
A. By 2000.
Q. I want to talk a little bit about what the company had available to it by 2002. Okay?

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A. Okay.
Q. We've seen a lot of reports from Pfizer going back and forth to EMEA in 2002. By 2002 and even earlier, the company had in its possession their own clinical trial data; is that fair?
A. Yes.
Q. The company had available to it the IMHS study data?
A. Yes.
Q. The company had available to it --
THE REPORTER: Could you slow down?
MR. OVERHOLTZ: Yes. I'm sorry.
(Reporter clarification.)
BY MS. LESKIN:
Q. And the company had available to it the PIM data?
A. 2002. Yes.
Q. Okay.
A. Yes.
Q. Are you aware that Pfizer has told the FDA that their marketing data shows that the average use of Viagra in their patients is approximately two to three times per month?
A. Per month, is that -- per month, right.
Q. Do you remember some questions regarding

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Pfizer's publication of the Gorkin report --
A. Yes.
Q. -- or your testimony regarding that?
A. Yes.
MS. LESKIN: Objection. I didn't ask anything about Gorkin.
MR. OVERHOLTZ: I said -- I changed it to her testimony.
MS. LESKIN: Okay.
BY MR.. OVERHOLTZ:
Q. Do you recall you mentioned of publication --
A. I did.
Q.. -- of a Gorkin report?
A. I did mention it.
Q. And you're aware of Pfizer's publication of the Gorkin report in 2006?
A. I am.
Q. And in that report, Pfizer pooled data from the clinical trial database and the PIM database to report an incidence rate of NAION associated with Viagra?
A. Yes.
Q. And you're aware that as early as 2002, Pfizer were reporting to various agencies and doctors the same pooling of data information --
A. Correct.

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Q. -- that was published in the Gorkin study?
A. Correct.
Q. Okay. Was it appropriate for Pfizer and Pfizer's employees to pull the clinical trial and PIM data to report an incidence rate for Viagra and NAION?
MS. LESKIN: Objection; outside the area of expertise. She's testified she's not an epidemiologist.
JUDGE BORG: Overruled.
MS. LESKIN: It's also outside the scope of the opinion that she's providing in this case. It's not anywhere in her report, and she didn't testify to that.
JUDGE BORG: How about some more foundation on that.
MR. OVERHOLTZ: I thought I laid a foundation regarding -- regarding the pharmacovigilance and the information -- I mean, she asked a ton of questions regarding what Pfizer had done.
BY MR. OVERHOLTZ:
Q. Let me ask you this.
Do you recall questions from Ms. Leskin related to Pfizer's campaign to understate the risk of Viagra associated with NAION?
A. I do, yes.

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Q. And do you recall the questions regarding Pfizer's efforts to denigrate the McGwin study that had been published?
A. Yes.
JUDGE BORG: We need a tape change very quickly.
THE VIDEOGRAPHER: We're off the video record. (There was a discussion off the record.)
THE VIDEOGRAPHER: We are back on the video record.
MS. LESKIN: I had an objection to that last question.
JUDGE BORG: Yeah. Can I get the question, please? Or do you want to -- do you just want to restate it?
MS. LESKIN: I can tell you what the question was, if that helps.
MR. OVERHOLTZ: I said: "Do you recall the questions regarding Pfizer's efforts to denigrate the McGwin study that had been published?"
MS. LESKIN: And I object because I don't think I asked any questions about Pfizer's efforts to denigrate the McGwin study. I don't think there has been any testimony about Pfizer's efforts --
MR. OVERHOLTZ: Yes, you did.

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MS. LESKIN: -- to denigrate the McGwin study.
JUDGE BORG: Yeah. It's overruled. Go ahead.
BY MR. OVERHOLTZ:
Q. Do you recall those questions?
A. Yes.
Q. And was it your understanding that the Gorkin study that was published by Pfizer attempted to refute the findings that were found in the McGwin study?
A. Yes.
Q. And that the --
JUDGE BORG: Slow. Slow. Slow.
BY MR. OVERHOLTZ:
Q. Were you aware that the Gorkin study and the data presented in the Gorkin study were published to refute the information that was coming out that there was an association between Viagra and NAION?
A. Yes.
Q. And I had already asked you whether or not you were aware that Pfizer had pooled that data together in the publication of that Gorkin report, correct?
A. I do understand that, yes.
Q. Okay. Was it appropriate for Pfizer to pool the data from the clinical trial and the PIM study in attempting to report an incidence rate to somehow denigrate the information that was coming out regarding

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an associate between Viagra and NAION?
MS. LESKIN: Objection. There's nothing in her opinion as to -- in her report or the opinion she's expressed today stating that she is going to give an opinion about -- in criticism of the Gorkin report.
JUDGE BORG: You know what? I don't recall the answer to that. I'm going to overrule. I'm going to overrule it and let you ask the question, and if you're able to answer it.
BY MR. OVERHOLTZ:
Q. Let me ask you this. Can you answer the question?
A. Yes.
Q. Okay. Go ahead.
A. Yes. Generally data are not pooled when they come from such diverse areas of controlled clinical trial data and a pharmaceutical event monitoring study, an uncontrolled study. So, yes, it is unusual to pool those data.
Q. Let me ask you -- I had been asking you some questions regarding pharmacovigilance.
A. Yes.
Q. Is that correct?
A. Yes.
Q. And pharmacovigilance is a heavy topic of your

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report, correct?
A. Correct.
Q. And the fact that you have given opinions that the company has a duty to investigate any signal?
A. Correct.
Q. In conducting that investigation, is part of that investigation looking at data from previous clinical trials?
A. Yes. You can, yes.
Q. And can it also involve looking at data from prescription monitoring trials?
A. You can.
Q. Should the company look at everything that's available to it?
A. Absolutely, absolutely..
Q. In light of your opinion that there's a problem with pooling that data, is that -- is -- was there a problem with PIM -- the PIM data reporting an exposure time with respect to the patients that took Viagra?
MS. LESKIN: Objection. Again outside the area of expertise and beyond the area of her expert report.
JUDGE BORG: Overruled.
THE WITNESS: Yes. My understanding is that the usage rate of Viagra was, if a patient took it

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once, it was considered for the month. And we know that it isn't taken that way. So using that calculation, there would been a -- be a diminution, a dilution of the occurrence rate using that.
So, yes, I understand how it was done. And based on what they later told FDA about the actual usage of Viagra, it was -- it was an improper way of calculating it.
BY MR. OVERHOLTZ:
Q. You -- you hold a Ph.D. in pharmacology, correct?
A. Yes..
Q. And as a pharmacologist, you understand that sildenafil has an acute pharmacologic action on the body; is that correct?
A. Yes.
Q. The half-life of -- of Viagra, sort of in general, is about what?
A. Four. About four hours.
Q. Okay. And for -- even if five times, six times that is what? A day?
A. Day's use or day's exposure.
Q. And generally are you aware that an event that could potentially be associated with Viagra is not expected to have been caused by the drug unless it

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happens within 24 hours of ingestion?
A. That is my understanding, yes.
Q. And that's because the drug is gone out of the system?
A. Right.
Q. Is that right?
A. Yes. And it has an acute effect. Not only gone, but its effect is acute.
Q. So in light of -- in light of your review of the information that the PIM data would count a month of exposure if the patient records using the drug for that month -- well, let's strike that. Let me ask you this.
Would it ever be appropriate for Pfizer in attempting to determine an incidence rate of Viagra associated with NAION to count as the time of exposure to the drug days when the patient doesn't use the drug?
MS. LESKIN: Objection; beyond the scope of her expertise and beyond the scope of her report.
JUDGE BORG: Overruled.
THE WITNESS: No, I certainly don't think so. And I think that was even discussed when FDA and Pfizer were talking about the upcoming study.. And it was agreed that it would only be the day the drug was used.
BY MR. OVERHOLTZ:

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Q. In -- conducting their pharmacovigilance and analyzing the signal, you would not want to count as time exposed on a drug days in which the patients don't take the drug?
MS. LESKIN: Same objection.
THE WITNESS: No, I don't believe so.
JUDGE BORG: Overruled.
THE WITNESS: I'm sorry.
MR. OVERHOLTZ: Go ahead.
JUDGE BORG: That's all right.
THE WITNESS: No, I don't believe so. And that -- and -- and I believe that FDA agrees with that in their interactions with Pfizer on the current study.
BY MR. OVERHOLTZ:
Q. Okay. Just a couple more questions, Dr. Blume.
Could Pfizer have designed a case control study to look at the association of NAION and Viagra?
A. Yes.
Q. And is it your opinion that based on Pfizer's duty to conduct pharmacovigilance that they should have initiated such a study?
A. Yeah. Oh, yes. I think so, yes.
Q. And do you believe, in analyzing Pfizer's regulatory actions in this case, that Pfizer acted

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appropriately with respect to their delays in initiating such a study?
A. No, I don't think so.
Q. Do you recall some questions regarding underreporting of adverse event data?
A. Yes.
Q. Have you -- have you seen reports or seen literature that indicates that men who take Viagra may fail to inform their physicians that they've taken that drug?
A. I did see that in the Pfizer documents, yes.
Q. And do you believe that men who have suffered a visual event prior to this event being in the labeling may have failed to report their use of Viagra to their ophthalmologist?
A. I did --
MS. LESKIN: Objection; outside the area of her expertise and beyond the scope of her expert report. We're getting farfetched here.
JUDGE BORG: I'm sorry?
MS. LESKIN: She -- we're getting farfetched and far way from where her area of expertise is.
JUDGE BORG: Yeah. Okay. It's overruled. But I want to hear the question again.
BY MR. OVERHOLTZ:

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Q. Do you believe that men who have suffered a visual event prior to this being in the labeling for the product could have failed to report their use of Viagra to an ophthalmologist?
JUDGE BORG: It's overruled.
Do you understand, are you able to answer the question?
THE WITNESS: Oh, yes, yes. I understand the question.
And I understand from reading the records that that -- that was in the records that men -- men do not always share with their ophthalmologist their use of an erectile dysfunction drug.
BY MR. OVERHOLTZ:
Q. Okay. And we talked about your expertise here today with respect to a company's pharmacovigilance duties, correct?
A. Correct.
Q. In conducting that pharmacovigilance, does a company have a duty to look at the issue of underreporting --
A. Oh, yes.
Q. -- in analyzing their adverse event database?
A. Absolutely, absolutely.
Q. And so consideration of an issue such as men's

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failure to report their use of a recreational drug or drug like Viagra would be an important issue for a pharmaceutical company to look at?
A. Oh, of course, of course.
JUDGE BORG: Mr. Overholtz, I've got to slow you down again.
MR. OVERHOLTZ: Okay. Three more questions.
JUDGE BORG: Our court reporter is so nice that she won't do that, but.
BY MR. OVERHOLTZ:
Q. Do you recall --
MR. BECNEL: I have to tell Neil two questions or, I ask two questions, whichever is quicker.
JUDGE BORG: Well, go ahead and finish, Mr. Overholtz.
MR. OVERHOLTZ: Take a quick break and --
MR. BECNEL: Huh?
MR. OVERHOLTZ: We'll, take a quick little thing --
JUDGE BORG: Yeah. No, no. Go -- go ahead and finish, Mr. Overholtz.
BY MR. OVERHOLTZ:
Q. Do you recall questions regarding whether or not Pfizer had reported all of the adverse events they had received related to NAION to the FDA?

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A. Yes.
Q. Okay. Are you aware that -- of correspondence between Pfizer and the FDA in 2006 regarding two cases --
A. Oh, yeah.
Q. -- of ischemic optic neuropathy in the IMHS study that had previously not been reported to the FDA by Viagra --
A. Yes.
Q. -- by Pfizer?
A. I do recall that.
Q. In conducting this investigation, we talked about Pfizer went back and looked at their clinical trials and the post-marketing studies like IMHS and PIM in looking for -- and their adverse event database. Okay? Would it be appropriate, in light of the fact that this event was not in the labeling and -- prior to 2005, that when Pfizer went back to look at their clinical trials that they would actually look at the reports and the medical records related to abnormal -- abnormal vision to make sure there were no cases?
A. Yes, that would have been -- that would have been wise to do.
Q. Okay. And do you know whether Pfizer has

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conducted that analysis or not?
A. I don't know that they did that.
Q. Okay.
JUDGE BORG: Mr. Becnel, just to ask -- he has a couple of -- well, okay.
MR. BECNEL: That's not it. He was given one more. Do you want me to ask it first?
MR. OVERHOLTZ: Yeah, go ahead.
MR. BECNEL: All right.
CROSS EXAMINATION
BY MR. BECNEL:
Q. You're aware that Ms. Leskin talked to you about some animal models?
A. Yes.
Q. Of dogs, rabbits, and rats?
A. Yes.
Q. Concerning trying to find out a signal in -- in those animals; is that correct?
A. True, yes.
Q. Were those the appropriate animal models to use for something dealing with ocular injuries?
A. Well, they certainly didn't predict it in the case of -- of the Viagra. But my understanding overall is that for ophthalmic tests in tracking ability to see, the only animal model that may be useful is --

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are monkeys.
Q. And that's what Dr. Hayreh did in all of his --
A. Yeah.
Q. -- investigatory work?
A. That's my understanding.
Q. Thank you.
A. But across all products. I'm talking not just erectile dysfunction drugs.
MR. BECNEL: That's it.
JUDGE BORG: Mr. Overholtz?
MR. OVERHOLTZ: That's it.
JUDGE BORG: Okay. Ms. Leskin, do you want any -- do you have anything else?
MS. LESKIN: Yeah. I have a few questions.
JUDGE BORG: Okay. Well, you have a few minutes left from your five.
MS. LESKIN: Can I expand that to 20? I don't think I'll need 20, but I'd like to expand that to 20 in light of some of the nonresponsiveness and colloquy on the record.
JUDGE BORG: I think 20 is a little heavy. I'll -- I'll give you -- I'll give you ten.
MS. LESKIN: Okay.
MR. OVERHOLTZ: I'm going to object to the ten.

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MR. BECNEL: Judge, we're going to --
MR. OVERHOLTZ: Move to strike anything after --
JUDGE BORG: I -- I know you do.
MR. BECNEL: We have other depositions to prepare for tomorrow.
JUDGE BORG: I understand.
MR. BECNEL: It's -- it's -- we have a court reporter who is exhausted. It's 7:00 o'clock. We've been here for nine hours with --
JUDGE BORG: I know.
MR. BECNEL: -- virtually no breaks.
JUDGE BORG: And the more we talk about objecting, the more everybody gets tired. So ten more minutes, and then we're done, unless you have something.
MR. OVERHOLTZ: And I'd just reserve an objection to later file in the court a motion to strike any of this testimony after this.
JUDGE BORG: You know, have at it. We've had a witness -- this witness has not been responsive on the direct from Ms. Leskin. That's eaten up a lot of time.
So, Ms. Leskin, you've got ten minutes.
MS. LESKIN: Thank you.

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REDIRECT EXAMINATION
BY MS. LESKIN:
Q. Dr. Blume, you said that you applied the methodology in this litigation that you use in connection with your pharmaceutical clients in nonlitigation, correct?
A. Yes.
Q. For your nonpharmaceutical -- for your nonlitigation clients, do you review internal documents?
A. Yes.
Q. Internal e-mails and internal minutes of meetings?
A. Well, I don't always receive their internal e-mails, but I'm generally at the meetings that deal with their NDA submissions.
Q. And is part of your responsibility analyzing those internal e-mails and memos regarding the intention or strategy for them on the marketing front?
A. Oh, those I'll -- I may see. Yes, those I'll see, especially if it relates to the adequacy of their -- or the appropriateness of their current marketing or their planned marketing relating to either their labeling or ongoing studies that they have. Now, those I may see.
Q. You were asked about Dr. Osterloh's 2002 report

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to the EMEA. Do you recall those questions?
A. Yes.
Q. And do you recall that Mr. Overholtz asked you whether the conclusion that Dr. Overholtz reached about not being able to exclude the possibility?
MR. BECNEL: You made a mistake because you're tired.
MS. LESKIN: Yeah, that's probably right. And I don't have the document in front of me. So let me withdraw that question and fix that.
BY MS. LESKIN:
Q. Okay. We're on Exhibit 24.
MR. BECNEL: I'm glad you adopted it.
BY MS. LESKIN:
Q. And Mr. Overholtz referred you to the summary and conclusions that are on page 6. Do you recall that?
A. Yes. I'm here.
Q. And Mr. Overholtz asked you that -- whether that last sentence on Dr. Osterloh's report was sufficient to establish a signal meriting a change in the label. Do you recall that testimony and that question?
A. I recall he asked if that was a signal, and if they understood that there was a signal, whether for a -- for that event it would -- was necessary to amend

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the labeling. Yes, I understand that.
Q. Okay. And you told Mr. Overholtz that that sentence signaled a -- triggered a requirement to change the label at least by the time of the submission, correct?
A. Certainly in my opinion, yes.
Q. Okay.
A. For that event.
(Exhibit No. 28 was marked for identification.)
BY MS. LESKIN:
Q. Let me show you -- I'm going to give you Exhibit 28.
Have you seen this document before?
And for the record, this is a September 25th, 2002, telefax from the EMEA.
Have you seen this document before?
A. I don't recall seeing this.
Q. And you recall that -- and this postdates Dr. Osterloh's submission that we just talked about as Exhibit 24, correct? This is dated September 25th, 2002. This was submitted the same time as Dr. Barrett's report, which is dated June of 2002.
MR. BECNEL: To which I'm going to object. If it wasn't covered in direct and it wasn't covered in cross, how can we start introducing new documents at

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this point?
JUDGE BORG: Because I gave you latitude on scope, I'm going to let her do the examination. It's overruled.
You can proceed.
BY MS. LESKIN:
Q. Looking at the conclusion that the EMEA provides to Pfizer on that front page --
Do you see the conclusion as -- the paragraph there saying that "this is our conclusion"?
"We would like to inform you that the CPMC in its meetings held from 7 to 19 September 2002 concluded the following points."
Do you see that?
A. Yes.
Q. And CPMC says, "Considering the fact that the incidence in the PEM study is not in excess compared to the background incident of NAION, and assuming that only 5 to 10 percent of all cases are reported, this means an incident rate of 1.4 to 2.8 per 100,000 still in line with the background incidence. In view of these data it seems acceptable not to include NAION as a sildenafil-related adverse event and ask the MAH to carefully monitor the occurrence of NAION and if appropriate submit a Type II variation to add this

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adverse event to the SPC at the time of the next PSUR."
Were you aware of that conclusion reached by the EMEA?
A. I was aware of the conclusion. I don't specifically remember this document. But that doesn't impact what my opinion would be for the United States because the FDA specifically tells us that we are not to involve -- we are not to consider incidence rate in deciding on labeling inclusions for post-marketing adverse events.
MS. LESKIN: Objection; nonresponsive.
JUDGE BORG: It is nonresponsive. It's sustained.
BY MS. LESKIN:
Q. Were you aware of this conclusion by the EMEA?
A. Yes, I was aware of it for European labeling..
Q. You were asked by Mr. Overholtz whether it was reasonable to review the reports of blindness that had been received. Do you remember that question?
A. Yes.
Q. Do you know whether Pfizer did that?
A. Yes.
Q. Yes, they did that, correct?
A. I -- at least some of them, because they're -- they're listed in their reports.

Q. Doctor, you were asked some questions about whether men could have failed to report to their doctors that they had taken Viagra. Do you recall that?
A. Yes.
Q. Do you have any expertise in a man's willingness to disclose medication?
A. Just my personal life. I'm just referring to the records that I recall in this case where they were concerned that it would not be unlikely that a patient wouldn't think to talk about an erectile dysfunction drug while he was at his ophthalmology visit.
Q. Have you conducted any studies to assess how often men do or do not disclose their medications to -- to their doctors?
A. No. I was just referring back to the documents in this case that was concerned about that.
(Exhibit No. 29 was marked for identification.)
BY MS. LESKIN:
Q. There was some discussion about the Gorkin article. I'm going to hand you Exhibit 29, which is a copy of Gorkin.
And you've seen that before, correct?
A. Yes, I have.
Q. You were asked some questions about the pooling of data in the --

A. Yes.
Q. -- Gorkin study.
Where does the article say they've pooled data from different sources?
A. It says, "To determine the incidences of NAION receive -- in men receiving sildenafil, we reviewed safety data from the global clinical trials and European observational studies."
Q. Okay. And if you look at the next paragraph, it says, "A review of collective database of 103 double-blind or open-label trials of sildenafil conducted between 1993 and 2003" -- just skipping a little bit of the middle there -- "revealed no cases of reported or observed NAION in more than 13,300 patient-years of observation."
A. Correct.
Q. Right?
A. Correct.
Q. And the next paragraph talks about the International Men's Health Study, correct?
A. Correct.
Q. And at the bottom it says, "No cases of NAION were reported during 2,935 patient-years of follow-up," correct?
A. Correct.

Q. The paragraph after that talks about the PEM study, correct?
A. Yes.
Q. And at the bottom of that paragraph it says, "Based on the report of one NAION case in a total of 35,500 patient years of observation in the PEM, the adjusted incidence of NAION is estimated to be 2.8 cases per 100,000 patient years of exposure.."
So I ask you again: Where does it say that the data from those three databases was pooled?
A. Well, I don't recall talking about the pooling from the IMHS study.
Q. What pooling were you referring to, Doctor?
A. I was referring to the control clinical data and the PEM study. I did not refer to the IMHS.
Q. Okay. So where does it say that the PEM study and the clinical database were pooled?
A. Give me one second here.
It says, "Using extensive epidemiology data and the clinical trial data, we estimate an incident -- incidence of 2.8 cases per 100,000 patient-years."
So they -- there's an "and" in there with clinical trial date and extensive epidemiologic data.
Q. Where are you reading?
A. Under "Discussion," first line of the second

paragraph.
Q. But the 2.8 cases, where is that coming from?
A. "An incidence of 2.8 cases per 100,000 patient-years."
Q. And that's the same number that they got after analyzing the PEM data, correct?
A. Yes. But they -- well, it's the same number, but they added -- they pooled this together saying, "Using this, we have come up with that estimate."
Q. Did you review the deposition of Rachel Sobel in this case?
A. Yes.
Q. Does Rachel Sobel acknowledge that -- say anything about the pooling?
A. I recall that she said they did not pool in the IMHS.
Q. That's the only thing you recall?
A. Yes.
Q. Do you recall Dr. Sobel's testimony regarding the events that Mr. Overholtz classified as ION events from the IMHS data?
A. The two?
Q. Yes.
A. Yes, yes.
Q. And do you recall Dr. Sobel saying that there

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was no evidence that those cases were nonarteritic anterior ischemic optic neuropathy?
A. I recall that she said that.
Q. And you haven't looked at the cases themselves, have you?
A. No. I just recall that they found two later.
Q. Last set of questions, Doctor.
Logically a cause must precede an event in order for there to be an effect, correct?
MR. BECNEL: Objection. Cause?
JUDGE BORG: What's the objection?
MR. BECNEL: The objection is it makes no sense.
JUDGE BORG: Well, I -- do you understand the question, Doctor, and are you able to answer it?
THE WITNESS: I was just focusing on the last paragraph of this paper, where they talk about the incidences with -- they say when they -- the analysis of both the clinical trial data and the --
THE REPORTER: Excuse me. Slow down.
JUDGE BORG: Well, yeah. Poor court reporter. Can I have the question read back, please?
MS. LESKIN: "Logically a cause must precede an event in order for there to be an effect, correct?"
JUDGE BORG: Okay. Are you able to answer that

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question?
THE WITNESS: A cause must precede an effect for there to -- a cause must precede an event for there be an effect?
MS. LESKIN: I'll rephrase it.
MR. BECNEL: That's what I said, it --
BY MS. LESKIN:
Q. In order for --
JUDGE BORG: Well, that's why I asked the witness if she could --
BY MS.. LESKIN:
Q. Doctor, if you could put the document down so you can concentrate on my question.
THE REPORTER: One at a time. I can't get you all. I can't get you all.
MR.. BECNEL: You get ten minutes, and then we violate the rule.
JUDGE BORG: Well, we're getting a lot of objections here, too, and --
MR. BECNEL: But I didn't make up the question.
JUDGE BORG: It's over -- it's overruled. Get the last question in, Ms. Leskin.
BY MS. LESKIN:
Q. Logically the ingestion of a drug must precede the -- an event in order for that drug to have caused

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the event, correct?
A. The ingestion of a drug must precede the event in order for there to have caused the event? Did you use the word "cause"?
Q. Yes.
A. Well, I don't know if I worry about -- I don't know if I agree with cause, but the -- the drug must be ingested -- yes, I will agree that they must use the drug.
Q. Well --
A. I'm not going to agree that --
Q. If we're going to --
A. -- it indicates cause.
Q. That wasn't my question. Let me rephrase, then.
MR. BECNEL: Objection.
JUDGE BORG: Yeah, it's noted and it's overruled. Let's get the question asked and answered.
BY MS. LESKIN:
Q. If the allegation is that the drug causes an event, the drug must have been taken before the event occurred, correct?
A. Yes.
Q. An event that occurs before the drug is taken

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could not have been caused by the drug, correct?
A. I think that's logical.
JUDGE BORG: Okay.. We're done.
MR. ALTMAN: I just have two very quick.
JUDGE BORG: Okay, Mr. Altman.
MR. ALTMAN: Two very quick questions.
RECROSS EXAMINATION
BY MR.. ALTMAN:
Q. We were talking about Dr. Osterloh's submission to the -- submission to the EMEA, correct?
A. Yes.
Q. A little bit earlier.
That -- that submission was prepared by Pfizer, correct?
A. Correct.
Q. Without suggesting that Pfizer did something deceitful, is it possible that Dr. Osterloh could have made a mistake in how he assembled the information to present to the EMEA?
MS. LESKIN: Objection; calls for speculation.
JUDGE BORG: Overruled.
THE WITNESS: This is possible.
BY MR. ALTMAN:
Q. And the EMEA in rendering their opinion relied upon the accuracy of that document when they rendered

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their opinion?
A. Correct.
Q. Please pull Exhibit 28 for a second, and go to the second page.
Would you please read starting at the top and through the -- the italicized --
A. Uh-huh.
Q. -- sentence.
A. "It might also be possible to include a statement comparable to the statement concerning cardiovascular adverse events as these issues concerning population at risk and background incidences are quite comparable. A statement example, anterior ischemic optic neuropathy has been reported post-marketing in temporal association with the use of Viagra, could be added to the SPC."
Q. And the SPC is the equivalent of the --
A. Label.
Q. -- U.S. label --
A. Uh-huh.
Q. -- correct?
So the EMEA didn't say this is wrong, correct?
A.. No, no. They would have -- they would have agreed to that statement being added if Pfizer had chose to add it.

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MR. ALTMAN: Thank you. I pass.
MR. OVERHOLTZ: Okay. I have a couple questions, Dr. Blume.
RECROSS EXAMINATION
BY MR. OVERHOLTZ:
Q. In looking at the Gorkin study --
A. Right.
Q. -- that Ms. Leskin was showing you, can you look at the summary section at the top of the first page?
A. Yes.
Q. Can you -- can you look at the summary section of that document at the top of the page --
A. Yes.
Q. -- of the Gorkin study?
And there is a sentence there at the bottom of the first paragraph that says "based on clinical trial data."
A. I see it.
Q. Okay. Can you read that?
A. "Based on clinical trial data in more than 13,000 men and on more than 35,000 patient-years of -- of observation in epidemiologic studies, we estimated an incidence of 2.8 cases of NAION per 100,000 patient-years of sildenafil exposure."

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Q. And if you could turn with me to the -- it's patient 502. It's, like, the third page of the study, under the discussion section.
A. Yes.
Q. If you can read with me the sentence at the very bottom of the page, beginning with "rather." Right there, "Rather, rather than supporting an increased incidence of..."
A. Oh. "Rather than supporting an increase incidence of NAION associated with sildenafil use, this analysis of clinical trial and epidemiologic data representing approximately 52 -- 52,000 patient-years of observation indicates that the NAION incidence in men with ED who took sildenafil worldwide is consistent with the range of estimated NAION incidence in the general U.S. population."
Q. Do you believe it was appropriate to combine the years of observation from the clinical trial and the epidemiological data from the IMHS and PEM that represent 52,000 patient years of observation to indicate that there was the -- the -- the rate -- incidence rate of NAION was similar to background rate?
A. No, and not in the summary.
MS. LESKIN: Objection.
THE WITNESS: 2.8 cases per 100,000

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patient-years.
BY MR. OVERHOLTZ:
Q. Okay. And do you know in the clinical trials there were -- how many clinical trials were indicated in the Gorkin study? Is it 103?
A. 103..
Q. Okay. Do you know in each of those clinical trials if the frequency of exposure to Viagra was the same for all of the patients in those clinical trials?
A. Are you talking about per -- per day?
Q. Yes.
A. Yes, one per day.
Q. No. But do you know that everybody in the clinical trials took the pill every single day?
A. No.
Q. Same frequency?
A. No.
Q. Do you know if the -- the authors from Pfizer who published this study adjusted for the different frequency of exposure rates within the 103 different clinical trials?
A. Oh, if they did, I have not seen that.
Q. Okay. And do you know if they did any type of adjustment related to the frequency of exposure to the drug in the PEM data?

A. No. They didn't.
Q. Would it have been appropriate to have done such an adjustment?
A. Yeah -- well, we now -- yes, of course. And FDA has affirmed that to them.
MR. OVERHOLTZ: Okay. Thank you. That's all we have.
THE VIDEOGRAPHER: We're off the video record.
THEREUPON, the deposition of CHERYL BLUME, Ph.D., taken at the instance of the Defendant Pfizer Inc., was concluded at 7:21 p.m.

CERTIFICATE OF DEPONENT

I have read the foregoing transcript of my deposition and except for any corrections or changes noted on the errata sheet, I hereby subscribe to the transcript as an accurate record of the statements made by me.

_____
CHERYL BLUME, Ph.D.

SUBSCRIBED AND SWORN before and to me this ____ day of _____, 20___.

_____
NOTARY PUBLIC

My Commission expires:

ERRATA SHEET
VERITEXT REPORTING COMPANY
1350 BROADWAY
NEW YORK, NEW YORK 10018
212-279-9424
CASE: VIAGRA PRODUCTS LIABILITY LITIGATION
DEPOSITION DATE: FEBRUARY 12, 2009
DEPONENT: CHERYL BLUME, Ph.D.

PAGE	LINE(S)	CHANGE	REASON

_____
CHERYL BLUME, Ph.D.

SUBSCRIBED AND SWORN TO BEFORE ME
THIS ___ DAY OF _____, 20__.

_____ _____
(NOTARY PUBLIC) MY COMMISSION EXPIRES:

CERTIFICATE OF REPORTER OATH

STATE OF FLORIDA
COUNTY OF SARASOTA

I, the undersigned authority, hereby certify that the witness named herein personally appeared before me and was duly sworn on February 12, 2009.
WITNESS my hand and official seal this 23rd day of February, 2009.

_____
DONNA L. PETERSON, RDR, CRR
NOTARY PUBLIC - STATE OF FLORIDA
MY COMMISSION NO. DD668780
EXPIRES: 8-7-11

REPORTER'S DEPOSITION CERTIFICATE

STATE OF FLORIDA
COUNTY OF SARASOTA

I, Donna L. Peterson, Registered Diplomate Reporter, Certified Realtime Reporter, and Notary Public in and for the State of Florida at large, hereby certify that the witness appeared before me for the taking of the foregoing deposition, and that I was authorized to and did stenographically and electronically report the deposition, and that the transcript is a true and complete record of my stenographic notes and recordings thereof.

I FURTHER CERTIFY that I am neither an attorney, nor counsel for the parties to this cause, nor a relative or employee of any attorney or party connected with this litigation, nor am I financially interested in the outcome of this action.

DATED THIS 23rd of February, 2009, at Sarasota, Sarasota County, Florida.

_____

DONNA L. PETERSON, RDR, CRR